The Washington State Newborn Screening Program

Health Care Provider's Manual

Public Health Laboratories
Washington State Department of Health

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INTRODUCTION

Newborn screening is a *population-based*, preventive *public health* program that is carried out in every state in the United States and in many countries throughout the world. It enables early identification of selected disorders that, without detection and treatment, can lead to permanent mental and physical damage or death in affected children. The goal of newborn screening is to facilitate prevention of developmental impairments (such as mental retardation and neurological deficits), delayed physical growth, severe illness, and death through early detection and intervention.

Across the United States there are variations in the disorders for which each state screens. Infants born in Washington State are currently screened for phenylketonuria (PKU), congenital hypothyroidism (CH), congenital adrenal hyperplasia (CAH), galactosemia, biotinidase deficiency, homocystinuria, maple syrup urine disease (MSUD), medium chain acyl-CoA dehydrogenase (MCAD) deficiency, sickle cell disease and other hemoglobinopathies. Although testing is possible for many other disorders, Washington adds tests to the newborn screening panel only after careful consideration of the following criteria:

- Prevention Potential and Medical Rationale: Identification of the condition provides a clear benefit to the newborn - preventing delay in diagnosis; developmental impairment; serious illness or death.

- Treatment Availability: Appropriate and effective *screening*, diagnosis, treatment, and systems are available for evaluation and care.

- *Public Health* Rationale: Nature of the condition (symptoms are usually absent, such that diagnosis is delayed and treatment effectiveness is compromised) and *prevalence* of the condition justify *population-based screening* rather than *risk-based screening.*

- Available Technology: *Sensitive*, *specific* and timely tests are available that can be adapted to mass *screening*.

- *Cost-Benefit / Cost–Effectiveness*: Benefits justify the costs of *screening*.

Successful newborn screening requires collaboration between the State Newborn Screening Program, health care facilities (hospitals, local health departments, clinics), *health care providers* (pediatricians, family practice physicians, nurse practitioners, midwives), and families of newborns. The *Washington State Newborn Screening Program* is within the *Department of Health* and is located at the State Public Health

Laboratory in Shoreline. It is a coordinated system of *screening* services comprised of laboratory, follow-up, and support staff.

The laboratory personnel:

- receive and prepare specimens for testing;
- test and analyze each specimen;
- record all results and report non-normal results to the *follow-up* staff;
- evaluate and maintain in-house procedures and specimen quality; and
- incorporate new technologies by establishing protocol and evaluating the integrity of the *screening* tests before implementation.

The *follow-up* and support staff:

- provide appropriate follow-up and referral to providers for newborns with *abnormal screening test results* to ensure prompt *diagnostic* and treatment services;
- provide long-term *follow-up* and tracking of affected children to ensure continued access to appropriate comprehensive health care, including distribution of metabolic treatment products;
- verify *screening* for all newborns and act if screening is delayed;
- collect, analyze, and disseminate data on newborn screening requirements including clinical outcomes; and
- provide consultation, technical assistance and education of newborn screening to hospitals, health care professionals, families of affected newborns and the general public.

Achieved through the cooperative work of the above three groups, the responsibilities of the Washington State Newborn Screening Program are:

- Rapid, efficient *screening* of children born in the state for the four disorders above.

- Verifying that each newborn has had access to *screening* and if not, taking action to assure screening is available.

- Appropriate *follow-up* and referral to *health care providers* for newborns with *abnormal screening test results* to facilitate prompt *diagnostic* and treatment services.

- Consulting with *health care providers* regarding test implications and recommending follow-up actions.

- Long-term *follow-up* and tracking of affected children to evaluate outcomes of the program, improve effectiveness and promote continued access to appropriate specialty health care.

- Collecting, analyzing, and disseminating data on newborn screening requirements, including cost effectiveness of the system and health outcomes.

- Consulting, providing technical assistance, and education regarding all components of newborn screening to hospitals, health care professionals, families of affected children, and the general public.

The responsibilities of the health care facilities and providers are:

- Properly collecting, labeling, and handling of newborn screening specimens.

- Documenting the *screening* status of each patient.

- Responding quickly to information and specimen requests from the Newborn Screening Program.

- Promptly following up on infants requiring further testing to rule out or confirm a diagnosis.

- Providing parent education about newborn screening and referral to specialty care services as needed.

The responsibilities of the families are:

- Educating themselves about the newborn screening test that will be performed on the infant.

- Reporting to the *health care provider* the presence of a *family history* of any screened disorder.

- Responding quickly to requests from the *health care provider* or *Department of Health* for repeat *screening*.

- Working cooperatively with *health care providers* and institutions when required for *follow-up*.

This manual will explain the necessary collaboration between the Washington State Newborn Screening Program, health care facilities and providers to help make newborn screening successful. Included is information about the disorders detected by the program and answers to frequently asked questions about newborn screening, such as the availability of *expanded screening*, the effects of transfusions, and the storage of *newborn screening cards*. This manual is intended to answer many of the questions *health care provider*s generally have about the screening system. We hope that you will find this information helpful.

This manual is provided as a courtesy to *health care provider*s in Washington State and is for informational purposes only. If you have any questions about information contained within this manual, please contact us by phone at (206) 361-2902 or by email at NBS.Prog@doh.wa.gov. When necessary, you will receive replacement sections to update the information contained in this manual. You may also access this and other information about newborn screening at our web site, http://www.doh.wa.gov/nbs.

HEALTH CARE PROVIDERS AND INSTITUTIONS SPECIMEN COLLECTION AND HANDLING

RESPONSIBILITY FOR OBTAINING A NEWBORN SCREENING SPECIMEN

Washington State law requires that every newborn be tested prior to discharge from the hospital or within five days of age. The law designates hospitals providing birth and delivery services or neonatal care to the newborn as being responsible for specimen collection. This includes informing the family of the purpose of *screening*, the legal requirement and the right to refuse. We recommend that physicians, midwives, and childbirth centers that deliver babies out-of-hospital follow the guidelines for hospital births.

PARENTAL RIGHT TO REFUSE

According to law (Chapter 70.83 RCW – PHENYLKETONURIA AND OTHER PREVENTABLE HERITABLE DISORDERS), a newborn screening specimen should not be obtained on any newborn infant "whose parents or guardians object thereto on the grounds that such tests conflict with their religious tenets and practices". If parents do refuse, it is the responsibility of the health care facility to obtain the signature from the parent(s) on the reverse side of the *screening card* to document the refusal. The provider must make certain that the parent(s) understand the risks of refusing the *screening*. As with collected specimens, the *demographic information* should be completed and the signed card forwarded to the Newborn Screening Program within 24 hours. The refusal should be noted in the infant's medical record.

It is important to note that religious reasons are the <u>only</u> valid basis for refusal. Newborn screening statistics indicate that the majority of infants whose parents signed a refusal in the hospital were later tested, indicating that the initial refusal was not truly based on religious principles. Affected infants could have a delayed diagnosis for several days or possibly weeks, thus placing them at significant risk of permanent damage or possibly death. The risk of refusal should be made clear to parents and refusals should not be accepted for any other reason.

TIMING OF SCREENING

In addition to the required first specimen, it is strongly recommended that every baby born in Washington have a second screening specimen collected between 7 and 14 days of age. This recommendation has been carefully considered relative to the specific disorders included in Washington's Newborn Screening Program. Laboratory detection of each of the nine disorders has its own special problems related to the ideal time for testing, hence the recommendation for two specimen collection times. Both the first and

second dried blood specimens receive the same battery of tests at the State Laboratory. The first screen is essential for making an early diagnosis necessary to prevent a salt-wasting crisis in a child with CAH, a fatal bacterial infection in a baby with galactosemia or a fatal metabolic crisis in a baby with MSUD. The second optimizes detection of PKU, CH, and homocystinuria, which rely on time-dependent changes in the concentration of substances in blood. Detection of hemoglobinopathies such as sickle cell disease is not dependent on the time of collection since testing relies on red cell components that do not change significantly during the first two weeks of life.

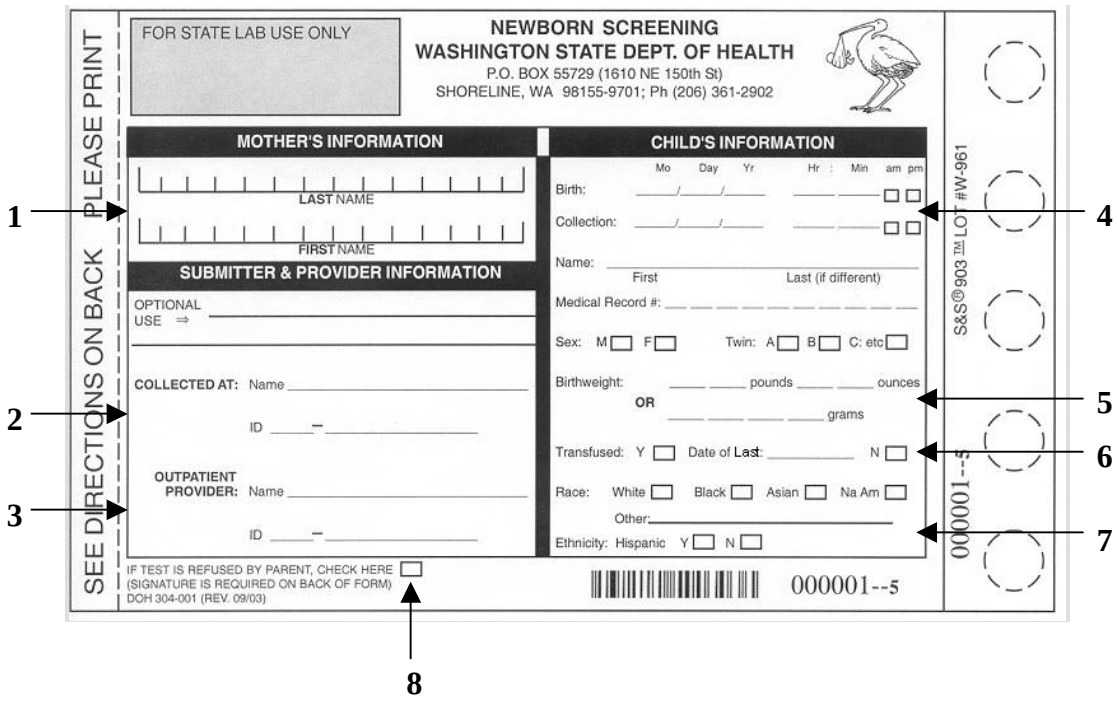
Aside from the fact that the hospital pre-discharge screen is mandated by state law, the practice of forgoing the first screen with the intent to collect a specimen at a later date to avoid "sticking the baby twice" is strongly discouraged. Besides greatly increasing the risk that a newborn screening specimen will not be obtained (because some infants will not return to the hospital or appear at a clinic), this practice unnecessarily delays diagnosis and treatment of affected infants, the majority of whom will be detected by the first *screening*, regardless of the disorder.

We are aware that, due to the increasing trend of early hospital discharge, the first well-baby visit with the primary *health care provider* is also being scheduled earlier. The standard of care for collecting the second specimen is still 7-14 days. However, in view of the increasing frequency of earlier first visits and possible uncertainty that the child will not be seen during the 7-14 day period, we are now recommending obtaining blood for the second newborn screen at the first well-baby visit, provided it is at least 48 hours after collection of the first specimen and it is a hardship for the baby to return to the hospital or clinic again between 7 and 14 days.

COMPLETING THE SPECIMEN CARD

It is extremely important that all requested information on the specimen card be filled out completely and accurately. This information is critical to interpreting the test results and facilitating rapid communication of results back to the submitter. Please contact the Newborn Screening Program at (206) 361-2902 to order specimen cards free of charge. A pamphlet for parents and a mailing envelope is also provided with each specimen card ordered.

Print all information using black or blue ink and stay within the limits of the designated boxes. Try to avoid touching the filter paper while completing the form as this could affect the results. A copy of the current card is below:



While all fields of the *newborn screening card* are important, we have noticed problems with compliance in the following areas as numbered above.

1. The mother's first and last names are used to link the first and second newborn screening specimens at the Newborn Screening Program. This linking may not occur if this information is different on the two *specimen cards*. Without this linkage the Newborn Screening Program may contact the *health care provider* unnecessarily to collect an additional specimen. Please be sure to use the mother's last name in this section if mother and child have different last names. If the mother's name is too long to fit into the boxes provided, continue printing the name outside of them.

2. The submitter listed on the *specimen card* is the health care facility or provider that collected the specimen and will receive the results after *screening*. Please write both the full name and the ID number. The ID numbers for hospitals are listed on the back of the *screening card*. For other ID numbers please contact our office at (206) 361-2902.

3. Rapid *follow-up* of an *abnormal screening test* depends upon identifying the *health care provider* who is caring for the child. This provider should be the one that the child will be seeing for primary care, such as a pediatrician, rather than the provider who cared for the child after birth, such as a neonatologist. Every effort should be made to ensure that the primary *health care provider's* information is accurate and complete. Please list both the name and the ID number of the provider. Please contact our office at (206) 361-2902 if you are not certain of your provider number. Some providers do not have an ID number (i.e. medical residents or fellows). In this case, please write the name of the facility that will be providing follow-up care in either this section or the Optional Use section.

4. The age of the infant at the time of collection is important in the interpretation of the *screening* results. The date of birth and date of collection should include the month, date, and year as well as the time of day.

5. Birth weight should be entered in either pounds or grams (preferably in grams), but not both. Please indicate the weight of the child at birth, rather than the weight of the child at the time of specimen collection. This information is important in the interpretation of the *screening* results.

6. The transfusion status of the child effects the *screening* results, particularly that of galactosemia and hemoglobinopathies. If the child has had a transfusion, please indicate on the card the date of the most recent transfusion. When this box is checked, the *screening* results will not contain information on hemoglobin or galactosemia, as it will not be accurate. For more information on how transfusion status affects *screening*, please see page 20.

7. For the child's race, check all that apply. Include Aleut and Eskimo under Native American and all of the following under Asian: Asian Indian, Cambodian, Filipino, Guamanian, Hawaiian, Japanese, Korean, Laotian, Samoan, and Vietnamese. The guidelines for assigning race are also listed on the back of the newborn screening collection card. In addition to race, please indicate whether or not the child is of *Hispanic* ethnicity.

8. If a parent or guardian refuses the newborn screening test, please check the box at the bottom of the card and have the parent or guardian sign the back of the card. In this case, please complete the information on the card as you would if blood had been collected. For more information on refusals, please see page 7.

SPECIMEN COLLECTION

The following specimen collection instructions are based on the approved standard published by *NCCLS* (*National Committee for Clinical Laboratory Standards*). If you have any questions regarding other techniques, please contact us at (206) 361-2902.

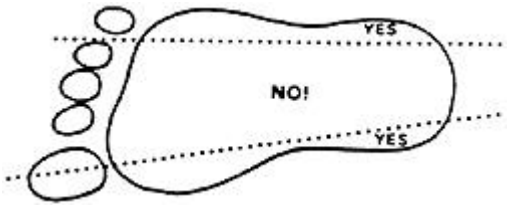
The following equipment will be needed for specimen collection: a sterile, disposable lancet with a depth less than 2.0 mm, a sterile 70% isopropyl alcohol pad, sterile gauze, a soft cloth, the blood collection form, and gloves.

Gloves should be worn for personal safety. To prevent specimen contamination, do not touch the blood collection filter paper circles with gloved or ungloved hands, alcohol, formula, water, powder, antiseptic solution, lotion, or other substances.

After confirming the identity of the infant, place the infant's feet lower than the level of the heart in order to increase blood flow to the foot. To increase the blood flow at the

puncture site, warm the heel for three to five minutes using a moist towel at a temperature no greater than 41°C. (Temperatures greater than this can burn the infant's skin.)

Select the puncture site. This should be the lateral or medial plantar surface of the heel, illustrated below.



Do not use previous puncture sites or the area at the heel curvature. The puncture must not be performed on the central area of the foot. This may result in damage to the nerves, tendons, and cartilage of the foot.

Cleanse the puncture site with the sterile alcohol pad and allow the heel to air dry. Using the sterile lancet, perform a swift clean puncture. Wipe away the first drop of blood with a sterile gauze pad. Allow another large drop of blood to form. To enhance blood flow, apply very gentle intermittent pressure with the thumb to the area surrounding the puncture. Avoid excess squeezing or "milking" as it contaminates the blood sample with tissue fluid.

Lightly touch the blood drop to the filter paper circle and allow a sufficient quantity of blood to soak all the way through the paper to completely fill the circle. Do not press the paper against the puncture site. Apply blood to one side of the filter paper only and allow full saturation before continuing with the next circle. Do not apply successive drops of blood to the same circle. If a circle cannot be filled due to diminished blood flow, repeat the procedure on a new circle. Repeat this until all circles are filled. It is important that complete saturation occurs for each circle due to the quantitative measurements used during *screening*. Results are based on a specific blood quantity within a particular sized sample. When blood does not soak completely through, the results are not comparable to lab standards and will be returned to the submitter as *unsuitable*.

After blood collection, elevate the foot above the body and gently press the puncture site with a sterile gauze pad or cotton swab until the bleeding stops.

Although the heel stick procedure is preferable, use of sterile heparinized capillary tubes for blood collection is acceptable. (Obtaining blood from an infant's finger is not an acceptable method of collection.) Follow the above procedures and apply approximately 75-100 µl to each circle, using a new tube for each circle. Touch the tube to the formed blood drop and apply a single application immediately to the paper. Do not touch the capillary tube to the filter paper when applying the blood; this will scratch or abrade the sample invalidating it for *screening*. (Note: the blood sample must not be applied to the filter paper as EDTA or citrate blood due to the chelating effect on europium.)

Blood collection from the dorsal hand vein is also an acceptable blood collection technique. However, do not use a vein into which IV fluids or blood are being or have been infused since this will contaminate the specimen. After venipuncture, follow the step outlined above for the heel puncture.

SHIPPING SPECIMENS

Allow the blood to air-dry on a flat, clean non-absorbent open surface for at least three hours at ambient temperature. Keep the specimen away from direct heat or sunlight and do not refrigerate the specimen. Do not store in a plastic bag as this invalidates the specimen due to unknown effects of condensation and degradation of the blood. When completely dry, merely fold (**do not tape or staple**) the flap with the biohazard label over the blood circles and double check that all information has been completed.

Place the card into the envelope provided. If sending more than one specimen, we recommend using an envelope for each card; otherwise, alternate the cards so that the blood specimens do not come into contact with one another. (Please do not place more than six collection cards in a single envelope.)

As required by law, send specimens to the Newborn Screening Laboratory **within 24 hours** of collection. Do not "*batch*" specimens from several days as this can significantly delay diagnosis of an affected child and may result in specimens being too old to test when they arrive.

For high priority specimens (i.e., infants with relatives affected with a disorder screened or those needed to confirm a clinically significant finding), overnight shipment is available via Federal Express. Call us at (206) 361-2902 to arrange for this shipping.

RESPONDING TO RESULTS

Screening results will be sent to the submitter of the specimen. These results are to be used as a record for the child's medical chart. Please carefully read the results for each child to verify that the specimen was suitable for testing and that no further testing is necessary. This information should ideally be forwarded to the child's *health care provider*, especially if the results were *abnormal* or *unsuitable*. Please see page 14 for more information on result categories.

REQUESTING RESULTS

If the results are not received for a specimen that you submitted within three weeks, please contact the Newborn Screening Program at (206) 361-2902, or fax your request to (206) 361-4996. Before calling, however, please verify that the results have not been misfiled, for example, under the mother's name.

If you are requesting results for a specimen that you did not submit, i.e., to verify that a first or second test has been done, please contact the health care facility or provider that submitted the specimen, if known, prior to contacting the Newborn Screening Program.

NEWBORN SCREENING PROGRAM
REPORTING RESULTS AND FOLLOW-UP

REPORTING RESULTS

Screening results fall within three broad categories: *normal*, *abnormal*, and *unsuitable*. Results are typically mailed within five days of the Newborn Screening Laboratory receiving the specimen. Over 90% of the results will be mailed within five days, while over 99% will be mailed within seven days. These results will be sent to the submitter of the specimen. If you receive a result report or letter that does not belong to a patient within your facility, please mail or fax the results to the Newborn Screening Program indicating such (See Appendix B for contact information).

Normal Results

Normal results will be sent to the submitter to be placed in the child's medical record. It is important to note that *normal* findings on the first test should not prevent a second specimen from being collected. As previously mentioned, the first screen is essential for making an early diagnosis necessary to prevent salt-wasting crisis in a child with CAH, a fatal bacterial infection in a baby with galactosemia or a fatal metabolic crisis in a baby with MSUD, and the second optimizes detection of PKU, CH, and homocystinuria, which rely on time-dependent changes in the concentration of substances in blood. In addition, if a child with *normal findings* develops clinical symptoms, the *screening* results should not prevent further testing.

Abnormal Results

Abnormal screening results include *borderline* and *presumptive positive* levels of *analytes* for PKU, CH and CAH, galactosemia, biotinidase deficiency, homocystinuria, MSUD, MCAD deficiency, as well as hemoglobin disorders and traits. The Newborn Screening Follow-up staff temper the response to abnormal test results by the degree of abnormality and the *demographics* of the infant. For instance, abnormal results are often secondary to prematurity or early sampling (<24 hours of age). A second specimen is usually all that is required to rule out the presence of one of the disorders screened.

For *borderline* levels or hemoglobin trait results, results are immediately mailed to the submitter with a request for a follow-up screen. If a second specimen is not received within two to four weeks, the child's primary *health care provider* will be contacted.

In the event of significant abnormal results, such as *presumptive positive* levels or a clinically significant hemoglobin disorder, the primary *health care provider* (as indicated on the *screening card* or by Medical Records at the child's facility of birth) is immediately contacted and appropriate recommendations for further testing are made. This may involve submitting another newborn screening specimen or following up with

diagnostic testing and referral to a medical specialist. All abnormal results are also reported by mail to the submitter with a note indicating the *follow-up* actions taken.

Unsuitable Specimens

The Newborn Screening Program receives some specimens that are *unsuitable* for testing. While the laboratory does test *unsuitable* specimens for extreme values when possible, improper collection compromises the accuracy of the test results. This delays the *screening* and diagnosis of the newborn and requires that a repeat specimen be submitted as soon as possible. Please see Appendix A for the various causes of *unsuitable* specimens.

REPORT FORMAT

The following two pages contain an example of the format in which results are mailed to submitters. These reports are mailed to the submitter upon completion of laboratory testing.

The first page contains the results for an individual child. The *State lab number* for that child is listed on the top left and is followed by the *demographic information* as completed on the newborn *screening card* by the submitting facility. The next section contains the *screening* results for the nine disorders, including the laboratory result and the classification.

The second page contains more detailed information on non-normal results and is not present for most results. It may contain further interpretation of the result, recommendations for follow-up, and actions taken by the Newborn Screening staff. It is important that this page be stored with the results on the previous page.

-EXAMPLE-

Washington State Department of Health
Public Health Laboratories

NEWBORN SCREENING PROGRAM LABORATORY RESULTS

PO Box 55729
Shoreline, WA 98155-0729
(206) 361-2902

NEWBORN SCREENING REPORT

STATE LAB #: 20040019999 **TESTING COMPLETED: 06/01/2004**

CHILD'S INFORMATION

Name: BABY DOE

Birth Date: 01/20/2004

Sex: FEMALE Birth Weight: 03500 gms

Medical Record #: 12345678

Collection Date: 06/02/2004

Age at Collection: 1 day(s) 15 hour(s)

Transfused: No

MOTHER'S INFORMATION

First Name: DOE

Last Name: JANE

SUBMITTER & PROVIDER INFORMATION

Collected at: H00XX

HOSPITAL NAME

Outpatient Provider:

Dr. John Smith

Optional Use:

Notes from hospital about any special circumstances (adoption, transfer, etc..)

NEWBORN SCREENING RESULTS

DISORDER	RESULTS	COMMENT	NORMAL RANGE
Congenital Hypothyroidism (CH) *TSH: µIU/mL serum*	27.10	Abnormal* - See Attachment	TSH<=34.4, 29.4, or 19.4 µIU/ml*
Congenital Adrenal Hyperplasia (CAH) *17-OHP: ng/mL serum*	26.77	NORMAL FINDINGS*	< 60.0 ng/mL
Hemoglobinopathy *Phenotype*	FA	NORMAL FINDINGS*	FA
Biotinidase *Enzyme Activity*	NORMAL	NORMAL FINDINGS*	Full Enzyme Activity
Galactosemia *Enzyme Activity*	NORMAL	NORMAL FINDINGS*	Full Enzyme Activity
Homocystinuria *Methionine : µmol/L blood*	< 80	NORMAL FINDINGS*	< 80 µmol/L blood
MCAD Deficiency *Octanoyl carnitine(C8) :µmol/L*	< 0.5	NORMAL FINDINGS*	< 0.5 µmol/L blood
Maple Syrup Urine Disease (MSUD) *Leucine : µmol/L blood*	< 300	NORMAL FINDINGS*	< 300 µmol/L blood
Phenylketonuria (PKU) *Phenylalanine : µmol/L blood*	< 180	NORMAL FINDINGS*	< 180 µmol/L blood

Based on child's age, birthweight, or transfusion status.
All infants should have a second newborn screen between 7 and 14 days to maximize detection of the disorders screened. Repeat screening is especially important for this infant either because the specimen was collected before 24 hours of age or the child had a very low birth weight (<1500g). Each of these factors can reduce the sensitivity of screening tests.

-EXAMPLE-

Washington State Department of Health
Public Health Laboratories

NEWBORN SCREENING PROGRAM LABORATORY RESULTS

PO Box 55729
Shoreline, WA 98155-0729
(206) 361-2902

STATE
LAB NO. 20040019999

TESTING
COMPLETED 06/01/2004

BORDERLINE THYROID

Most borderline results are due to factors other than congenital hypothyroidism (i.e. early collection, low birth weight, clinical status). However, to ensure that this infant does not have congenital hypothyroidism, another newborn screening specimen should be submitted promptly. Our follow-up staff will contact the child's health care provider if a subsequent specimen is not received. Please call our office at (206) 361-2902 or toll-free at 1-866-660-9050 if there are any questions regarding these thyroid results.

CHB.txt 6-1-04

REQUESTS FOR REPEAT SCREENING

When necessary, the Newborn Screening Program contacts *health care provider*s to advise that a repeat specimen be taken. This will occur if a previous specimen was *unsuitable* for *screening*. Although *unsuitable* specimens are analyzed for extreme *analyte* values (which could indicate the presence of a disorder), when a child's only specimen is *unsuitable*, a valid specimen will always be requested. Another screening specimen may also be requested if there was a previous *abnormal test result*. This does not necessarily mean that the child has one of the disorders screened, but that a subsequent specimen is needed to rule out or help establish the presence of a condition. If you receive a request for another specimen, please contact the parent or guardian as soon as possible to help facilitate the child to be rescreened.

REQUESTS FOR INFORMATION

The Newborn Screening Program sometimes receives *screening cards* with incomplete *demographic information* required for *follow-up*, such as the name of the primary care provider. To obtain this information, the hospital or other known *health care provider* is contacted. The information that is provided is kept confidential, as is the information on the *screening card*. Prompt responses to requests for information are appreciated.

SPECIAL CONSIDERATIONS

TRANSFUSIONS

The first newborn screening specimen should be obtained prior to transfusion whenever possible. Specimens collected following red blood cell transfusions will yield invalid results for galactosemia and hemoglobinopathy screening. In the event that the first screening specimen is collected after a transfusion, please note this on the *screening card* to assist the laboratory in interpreting the results and recommending *follow-up* procedures. The galactosemia status and hemoglobin phenotype can be determined after the transfused cells have cleared. A specimen collected four to six weeks after the last transfusion will resolve galactosemia disease status and hemoglobin phenotype in most circumstances. The first and second specimens should still be collected within the recommended times because the detection of the other seven disorders is not affected by the transfusion.

PREMATURE AND SICK INFANTS

The Washington State Newborn Screening Program recommends an additional specimen collection for sick and premature infants. This includes infants weighing less than 1500 grams at birth and sick infants requiring a hospital stay of three weeks or more. The standard of practice for newborn screening in Washington State is for all infants to have two heelstick specimens collected and sent to the State Public Health Laboratory for testing. The first specimen is mandatory and must be collected before discharge from the hospital or by five days of age if the infant remains in the hospital beyond the usual stay. The second specimen should be collected between seven and fourteen days of age.

Recent studies and our own experience in Washington State indicate that premature and sick infants with congenital hypothyroidism can have a late onset of thyroid stimulating hormone (TSH) elevation that may not be detected on the second specimen. It is thought that this delay may be caused by immaturity of the thyroid gland or receipt of transfusions and medications.

Because elevated TSH is the most specific screening indicator for congenital hypothyroidism, it is recommended that a third newborn screening specimen be collected from premature and sick infants between four and six weeks of age or just prior to hospital discharge, whichever is sooner. This specimen should be in addition to the two specimens recommended for all infants. There is no extra charge for the additional specimen; our one-time fee covers all testing that may be needed.

TRANSFERRED INFANTS

As the hospital of birth is legally responsible for the *screening*, that hospital should ensure that the facility of transfer is aware of the screening status. This should be documented in the infant's records at transfer. If there is no record of *screening*, a specimen should be obtained as soon as possible. This also applies to infants who are transferred to or from a hospital outside of Washington State.

PARENTS WHO DO NOT RESIDE IN WASHINGTON STATE

For infants who will not reside in Washington State after discharge from a Washington hospital, it is important that this is noted on the *newborn screening card* in addition to the name of the follow-up provider.

ADOPTIONS

For babies being adopted, please indicate the adoption agency or the infant's adoptive name (if known) on the *newborn screening specimen card* so they can be contacted if follow up is necessary. This information can be noted in the Optional Use section of the screening card. This expedites follow up when the first test has the birth mother's name and the second has the adoptive mother's name. In this situation, the two tests would not be linked and would be treated as two different infants. Information on adoptions will be kept confidential as is all information provided to the Newborn Screening Program.

INFANTS WITH CLINICAL SIGNS

As with all laboratory tests, newborn screening testing may yield *false negative* results. Regardless of the results of the newborn screen, the child's *health care provider* should proceed with *diagnostic testing* on any infant exhibiting clinical signs and symptoms. Please alert the Newborn Screening Program in this situation.

INFANTS WITH AFFECTED RELATIVES

For any infant with a relative affected with one of the newborn screening disorders, providers should alert the Newborn Screening Program so testing can be expedited. In addition, providers should contact an appropriate medical specialist, ideally prenatally, to determine if any *diagnostic testing* or *genetic counseling* is indicated.

SCREENING OLDER CHILDREN

Some children are not tested at birth, including those who immigrate into the United States. In addition, there may be children for whom *screening* status is not known, including children adopted from another state. We recommend that a specimen be obtained for these children at the first provider visit. *Screening* older children is valid for most of the disorders. It is very important that the date of birth be written on the card so that the results may be correctly interpreted.

SCREENING FOR DISORDERS NOT DETECTED IN WASHINGTON STATE

As previously mentioned, there are other disorders that may be screened for at birth that are not included in as part of the Washington State newborn screen. If the family is interested in obtaining *expanded newborn screening* beyond what we offer, there are laboratories that will perform testing on specimens for a small fee. Pediatrix Screening (866-463-6436),Baylor University Medical Center (800-422-9567), Mayo Medical Clinic (800-533-1710) and University of Colorado (303-315-7301) will perform supplemental screening for over 20 metabolic disorders using a kit ordered by providers or parents. Please contact them for further information.

STORAGE OF NEWBORN SCREENING CARDS

The Newborn Screening Program retains the specimen card for 21 years after the birth of the child. We retain these forms as a part of the child's health care records consistent with requirements for hospital records for minors. As health care information, these specimens are protected by confidentiality and cannot be used for purposes other than newborn screening without informed consent by the parents and/or child or by a properly executed subpoena (Chapter 70.02 Revised Code of Washington, Medical Records - Health Care Information Access and Disclosure). Such uses have included testing the specimen for a disease diagnosed in the child later in life.

NEWBORN SCREENING FEE

The Newborn Screening Program is a self-supporting fee based program. A fee is charged for each infant tested through birthing facilities. This is a one-time fee and is charged per infant screened, not per specimen. The fee funds all activities of this comprehensive program. *Diagnostic testing*, if necessary, will involve additional costs. For the current amount of the fee, please contact the NBS program or visit our website at www.doh.wa.gov/nbs.

DISORDERS

OVERVIEW

There are currently nine disorders screened for in the newborn in Washington State: phenylketonuria (PKU), congenital hypothyroidism (CH), congenital adrenal hyperplasia (CAH), galactosemia, biotinidase deficiency, homocystinuria, maple syrup urine disease (MSUD), medium-chain acyl-CoA dehydrogenase (MCAD) deficiency, and sickle cell disease and other clinically significant hemoglobinopathies.

PHENYLKETONURIA

Phenylketonuria (PKU) was the first disorder screened for at birth and marked the beginning of newborn screening. PKU is characterized by the inability to metabolize the essential amino acid phenylalanine due to the lack of the enzyme phenylalanine hydroxylase. If untreated, PKU results in severe neurological and developmental damage. Although the exact pathogenesis of the damage to the central nervous system is still not clear, it seems likely that an increased concentration of phenylalanine in the blood is associated in some way with the neurodegenerative effects. Treatment consists of a special diet low in phenylalanine. Affected infants develop normally with early identification and proper dietary management. The *prevalence* of PKU in the United States is approximately 1 in 10,000-25,000. In Washington State, there are, on average, seven infants with PKU detected each year.

Clinical Features

Infants with PKU appear normal at birth. The symptoms of untreated PKU develop gradually, so they may not be noticed until irreversible mental retardation has occurred. The most common symptoms of untreated PKU are a "musty" odor to the skin and urine, increased muscle tone and tendon reflexes, an eczema-like rash, and progressive neurological damage. With early treatment virtually all symptoms of the disorder are eliminated.

Etiology

PKU is caused by a genetic deficiency in the enzyme phenylalanine hydroxylase, which metabolizes the common amino acid phenylalanine. It is inherited in an *autosomal recessive* fashion.

Laboratory Tests

The PKU *screening* is no longer performed by the bacterial inhibition assay developed by Dr. Robert Guthrie, commonly known as the "Guthrie test." Screening is now done using a technology called tandem mass spectrometry (MS/MS). The levels of phenylalanine and tyrosine in the blood spot are measured by a tandem mass spectrometer. Infants are

considered to have a *presumptive positive* test for PKU when they have blood phenylalanine levels of 240 μmol/L (equivalent to 4 mg/dL) or more and a phenylalanine-to-tyrosine ratio of 2 or greater.

Laboratory Result Classifications and Corresponding Follow-up Actions for PKU

Analyte	**Normal Results**	**Borderline Results**	**Presumptive Positive**
Phenylalanine (μmol/L serum)	<180	180-239	>240
	Results are mailed to specimen submitter. No follow-up is required.	Health care provider is contacted by phone to recommend a repeat newborn screening specimen as soon as possible. Results are also mailed to submitter.	Health care provider is contacted immediately by phone to recommend a repeat newborn screening specimen and/or *diagnostic testing* as soon as possible. Results are also mailed to submitter.

Diagnostic Testing

A *positive* PKU *screening* result must be confirmed as part of a clinical evaluation before a diagnosis is made and treatment initiated. *Diagnostic testing* for PKU is done at Children's Hospital and Regional Medical Center's Biochemical Genetics Laboratory as part of the University of Washington PKU Program in Seattle (see Appendix C for contact information). The child can go directly to Children's Hospital or a blood and urine sample can be sent to their Clinical Laboratory. If *diagnostic testing* is recommended, the Newborn Screening Program will provide details on how the blood and urine should be collected.

Treatment

Early and proper initiation of a low-phenylalanine diet will prevent the mental retardation that occurs in untreated PKU. Strict dietary restriction of natural protein is required to reduce high blood phenylalanine levels. This is accomplished by the intake of a special metabolic formula (i.e. Phenyl-Free®) supplemented by low-protein foods and avoidance of aspartame (NutraSweet®). Treatment should be started as soon as the diagnosis is confirmed and should be continued indefinitely to optimize normal physical and mental development. Ongoing medical management with regular monitoring of phenylalanine levels is provided by a multidisciplinary team at the University of Washington PKU Clinic. The staff consists of a pediatric biochemical geneticist, nutritionists, a social worker, and genetic counselor. The special metabolic formula is distributed by the Newborn Screening Program under direction of the PKU Clinic.

Maternal PKU
As stated above, treatment for PKU should be continued throughout one's life. Discontinuing or even relaxing the dietary protein restriction may result in the late onset of clinical symptoms. It is especially critical that women of childbearing age maintain very strict dietary control. Women with high levels of phenylalanine during pregnancy are at increased risk of fetal loss, fetal brain damage, and other birth defects. If blood phenylalanine levels can be kept very low prior to conception and throughout the entire pregnancy, damage to the fetus can be minimized or avoided.

Offspring of women who have PKU may have a transient elevation of phenylalanine on their newborn screening test. This level will fall to normal within a few days, unless the child has PKU (a 1 in 200 chance).

False Negative/Positive
The *false negative* rate for PKU depends on the age at which the infant is screened. A small percentage will be missed if the *screening* is done very early (prior to 12 hours of age). In Washington State, approximately 96% of infants with PKU are detected on the first newborn screen. The *false positive* rate is also very low.

Special Considerations
The PKU *screening* test (by MS/MS) may yield equivocal results in babies who receive hyperalimentation or other therapeutic infusions. The result will be reported as an "inconclusive" and a follow up screen will be recommended when treatment is concluded.

Contrary to the common belief that infants must have at least 24 hours of feeding before the PKU test is accurate, feeding is <u>not</u> necessary for PKU detection. The majority of affected infants will be detected on the first screen, although milder forms of PKU may not be detected until the second screen.

CONGENITAL HYPOTHYROIDISM (CH)

Congenital hypothyroidism (CH) is characterized by the inability to produce adequate amounts of thyroid hormone, thyroxine (commonly known as T4). Proper production of T4 levels is critical for normal physical growth and mental development. If untreated, CH results in severe neurological and developmental damage. Diagnosis and initiation of appropriate synthetic thyroid hormone replacement (levothyroxine), within the first few weeks of life, followed by regular clinic visits with physicians experienced in the treatment of CH, can prevent growth failure and mental retardation. The *prevalence* of CH in the United States is approximately 1 in 3,500. In Washington State, there are, on average, 25 infants with CH detected each year.

Clinical Features

Infants with untreated CH usually appear normal until about three months of age, but it is likely that some brain damage will have already occurred. Clinical symptoms or signs, if present, include prolonged neonatal jaundice, constipation, lethargy, poor muscle tone, feeding problems, a large tongue, mottled and dry skin, distended abdomen, and umbilical hernia. These are not reliable indicators of CH, however, as they are non-specific for CH.

Etiology

The insufficient production of the thyroid hormone T4, which characterizes CH, is most commonly caused by the malformation or malfunction of the thyroid gland. This includes the total or partial failure of the thyroid gland to develop normally (athyreosis or hypoplasia), improper location of the gland (ectopic), or an enzyme deficiency or other chemical disruption in the pathway of thyroid hormone production (dyshormonogenesis). Other factors that can affect thyroid hormone function in an infant, and therefore result in an *abnormal screening result*, are prematurity and maternal medications such as antithyroid drugs or iodine.

Laboratory Tests

The newborn *screening* tests for CH are performed using a very precise chemistry technology called fluoroimmunoassay. The screening test for has recently changed from measuring the infant's thyroxine (T4) level followed by a TSH level (thyroid stimulating hormone) for those infants whose T4 levels fall in the lowest 10% of that day's assay to initially measuring TSH on all infants. A TSH above a certain value will be re-analyzed in duplicate before a classification is made. Infants are considered to have a *presumptive positive* result for CH if the TSH level is between 60-100 μIU/ml depending upon the baby's age when the blood specimen was collected.

Laboratory Result Classifications and Corresponding Follow-up Actions for CH

Analyte	**Normal Results**	**Borderline Results**	**Presumptive Positive**
TSH (μIU/ml)	<40 if <24 hrs <25 if ≥24 hrs	40-99 if <24 hrs 25-59 if ≥24 hrs	≥100 if <24 hrs ≥60 if ≥24 hrs
	Results are mailed to specimen submitter. No follow-up is required.	NBS waits for the routine second specimen. If not received within 2 to 4 weeks, health care provider is contacted to recommend newborn screening specimen as soon as possible. Results are also mailed to submitter.	Health care provider is immediately contacted by phone to recommend a repeat newborn screening specimen and/or *diagnostic testing* as soon as possible. Results are also mailed to submitter.

Treatment

Treatment of CH is relatively simple and very effective. Thyroid hormone, in a synthetic pill form (i.e., Synthroid®), is administered orally once daily. The dosage of medication must be adjusted and monitored as the child grows. Appendix C lists pediatric endocrinologists in Washington and Oregon who can be consulted for confirmation of diagnosis and treatment.

False Positive/Negative

False positives may occur due to early specimen collection. In the first day of life, TSH levels may be transiently elevated. In normal cases this level will resolve after the first 24 hours. In addition, premature infants may exhibit a physiological reduction in TSH levels. It is important that both of these types of cases receive follow-up to ensure that the thyroid levels return to the *normal range* as the infant matures.

The *false negative* rate for CH on the first newborn screening specimen is higher than for all of the other disorders screened. Washington's experience has been that about 15% of infants with confirmed CH were detected only after their second newborn screen when using primary T4 followed by TSH. Screening all infants for TSH will hopefully reduce this *false negative* rate on the first screen. The observed *false negative* rate is thought to be largely due to the residual thyroid hormone activity that was provided by the mother.

For maximum detection of CH alone, the recommended second newborn screen can be critical for an affected infant.

Special Considerations

Premature infants (birth weight less than 1500 grams) and sick infants have been documented to develop a late onset form of CH. It is therefore recommended that a third newborn screening specimen be collected for these infants between four and six weeks of age. Please see page 19 for more information on the recommended third newborn screen for premature or sick infants.

CONGENITAL ADRENAL HYPERPLASIA (CAH)

Congenital adrenal hyperplasia (CAH) is characterized by the excessive production of androgenic hormones due to lack of the enzyme 21-hydroxylase. If untreated, CAH can lead to an imbalance in the body's concentration of salts, which in turn can rapidly lead to shock and death. CAH also causes excessive masculinization and extremely premature sexual maturation. Treatment consists of cortisol, which normalizes hormone production. Proper treatment prevents death and stops the masculinization process. Affected females may require surgical correction of masculinized genitalia. The *prevalence* in the United States is approximately 1 in 18,000. In Washington State, there are, on average, four infants with CAH detected each year.

Clinical Features

Male infants with CAH usually appear normal at birth but develop symptoms within the first week of life. Female infants may show the effects of the virilizing hormones at birth. This usually presents itself as an enlarged clitoris and fusion of the labia majora over the vaginal opening. Occasionally the female infant may be so virilized at birth that an erroneous gender assignment is made. Such newborns should not have a palpable gonad in the labial/scrotal sac. Please alert the newborn screening program immediately if virilizing symptoms are present in an infant so that testing for CAH can be prioritized.

Since infants with CAH may experience a life-threatening salt-wasting crisis within the first week of life, it is critical that the first newborn screening specimen be collected and mailed according to the requirements (by five days of age).

Etiology

Several types of genetic defects cause CAH, all of which are inherited in an *autosomal recessive* fashion. The newborn screening test is designed to detect 21-hydroxylase enzyme deficiency, which is responsible for over 90% of CAH. Therefore, providers should remember that a normal newborn *screening* result does not rule out other forms of CAH due to other enzyme deficiencies. As with all disorders, providers should proceed with *diagnostic testing* if clinical symptoms are present despite the results of the newborn screening test, especially if a child only had one newborn screen and the simple virilizing form of CAH is suspected.

Laboratory Tests

CAH screening, like thyroid screening, is done by fluoroimmunoassay. Hormone levels of 17-hydroxyprogesterone (17-OHP) are measured, which is elevated in the blood of infants with the disorder. A 17-OHP level above a certain value will be re-analyzed in duplicate before a classification is made. Due to the variability of the disorder and the age of the infant, the level of 17-OHP may not correlate with the clinical severity of the disease.

Laboratory Result Classifications and Corresponding Follow-up Actions for CAH

Analyte	Normal Results	Borderline Results	Presumptive Positive
17-OHP (ng/ml)	If birth weight is ≥2500 gm, <60; if birth weight is <2500 gm, <90 if collected at <10 days or <60 if collected at ≥10 days	60-90 in infants tested at ≥10 days of age	≥90
	Results are mailed to specimen submitter. No follow-up is required.	Health care provider is contacted by phone to recommend a repeat newborn screening specimen as soon as possible. Results are also mailed to submitter.	Health care provider is contacted by phone to recommend a repeat newborn screening specimen and/or *diagnostic testing* as soon as possible. Results are also mailed to submitter.

Treatment

Treatment for CAH includes hormone replacement medication. Glucocorticoids (cortisone or hydrocortisone) can be given by mouth or injection. In the event of vomiting, serious illness, injury, or surgery, much higher doses are required. Mineralcorticoids are needed if the infant is unable to maintain normal levels of sodium and potassium. Over-medication can cause hypertension in some children, therefore blood pressure should be monitored. Medications need to be adjusted as the infant matures. Appendix C lists pediatric endocrinologists in Washington and Oregon who can be consulted for confirmation of diagnosis and treatment.

Females who have virilization of the genitalia may need surgical correction. The first surgery is usually done before two years of age and is done in stages.

False Positive/Negative

In the first day of life, 17-OHP levels may be transiently elevated. In normal cases this level will resolve after the first 24 hours. In addition, premature or ill infants may exhibit an elevation in 17-OHP due to physiological stress or administration of medications. It is important that the infant receive follow-up to ensure that the adrenal levels return to the *normal range* as the infant matures.

False negative results on a first newborn screen are usually the result of an infant who has the simple virilizing form of 21-hydroxylase deficiency. Although not a life-threatening disorder, these infants require a *diagnostic* work-up to determine the appropriate course of treatment.

BIOTINIDASE DEFICIENCY

Biotinidase deficiency is characterized by an inability to recycle the vitamin biotin due to lack of the enzyme biotinidase. If untreated, biotinidase deficiency can lead to irreversible neurological damage, metabolic crisis and even death. Treatment consists of administering oral doses of the vitamin biotin every day, typically 10 mg per day. Early diagnosis and proper treatment will avoid all damage. The *prevalence* of biotinidase deficiency in the United States is approximately 1 in 60,000.

Clinical Features

Infants with biotinidase deficiency appear normal at birth but signs of the disorder begin to emerge anywhere from a few weeks to several years. Affected children initially show combinations of neurologic and cutaneous symptoms, including seizures, ataxia, hypotonia, developmental delay, hearing loss, decreased vision, rash, conjunctivitis, and fungal infections. Death may even occur due to severe metabolic decompensation.

Etiology

Biotinidase deficiency is caused by a genetic deficiency in the biotinidase enzyme, which recycles the common vitamin biotin by cleaving it from lysine residues in certain proteins. Biotinidase deficiency is inherited in an *autosomal recessive* fashion.

Laboratory Tests

Biotinidase deficiency screening is done by a colorimetric assay. Activity of the enzyme biotinidase, which is reduced in infants with this disorder, is measured. A diminished color in the processed blood specimen indicates that the infant may have biotinidase deficiency.

Laboratory Result Classifications and Corresponding Follow-up Actions for Biotinidase Deficiency

Analyte	Normal Results	Borderline Results	Presumptive Positive
Biotinidase Enzyme (% activity)	>30%	10% - 30%	<10%
	Results are mailed to specimen submitter. No follow-up is required.	NBS waits for the routine second specimen. If not received within 2 to 4 weeks, health care provider is contacted. Results are also mailed to submitter.	If first screen, health care provider is contacted by phone to recommend immediate second specimen. If second screen, immediate diagnostic testing is recommended.

Treatment

Treatment for biotinidase deficiency is a 10 mg oral dose of the vitamin biotin every day. Early diagnosis and treatment before the onset of symptoms can avoid all negative consequences of the disorder. Treatment after onset will resolve some symptoms but will not reverse neurological damage.

False Positive/Negative

The enzyme evaluated in screening is prone to damage if the sample is delayed in the mail or exposed to high temperatures. This may cause a false positive result.

GALACTOSEMIA

Galactosemia is characterized by the inability to metabolize the sugar galactose due to decreased activity of the enzyme galactose-1-phosphate uridyltransferase (GALT). If untreated, galactosemia results in severe neurological and developmental damage and often neonatal death due to E. coli sepsis. Treatment consists of immediately eliminating dietary intake of lactose by replacing breast or normal formula milk with a lactose-free, soy-based formula. Antibiotics are also prescribed to prevent sepsis. The *prevalence* of galactosemia in the United States is approximately 1 in 50,000.

Clinical Features

Infants with galactosemia usually appear normal at birth, but soon develop signs of the disorder after they begin feeding on milk. Symptoms may include a failure to thrive and vomiting or diarrhea after ingesting milk. Hepatomegaly and jaundice are common by the end of the first week of life. Infants who survive untreated may develop liver disease, kidney damage, cataracts, growth failure, mental retardation, and ovarian failure in girls. Many of the problems associated with galactosemia can be prevented if the baby is diagnosed and treated early by switching to a soy-based formula and eliminating galactose and lactose intake for life.

Etiology

Galactosemia is caused by a genetic deficiency in the enzyme galactose-1-phosphate uridyltransferase (GALT), which helps metabolize the sugar galactose. It is inherited in an *autosomal recessive* fashion.

Laboratory Tests

Galactosema screening is done by a fluorometric assay. Activity of the enzyme GALT, which is reduced in infants with this disorder, is measured. A diminished fluorescence in the processed blood specimen indicates that the infant may have galactosemia.

Laboratory Result Classifications and Corresponding Follow-up Actions for Galactosemia

Analyte	**Normal Results**	**Borderline Results**	**Presumptive Positive**
GALT (Units/ gHb)	>2.5	2.1-2.5	≤ 2.0
	Results are mailed to specimen submitter. No follow-up is required.	If first screen, health care provider is contacted by phone to request routine second specimen. If two abnormal screens, diagnostic testing is recommended.	Health care provider is immediately contacted by phone to recommend substitution of soy formula for breast milk or commercial based formula and prompt diagnostic testing.

Treatment

The main treatment for galactosemia is the elimination of galactose and lactose from the diet. Dietary management needs to begin as soon as possible and continue throughout life. Once diagnosed, the infant should be changed to a soy-based formula that does not contain galactose. Antibiotics are normally prescribed to prevent sepsis, even after a child has been switched to a soy-based formula, as sepsis can still arise if the child has previously ingested galactose.

False Positive/Negative

The enzyme evaluated in screening is prone to damage if the sample is delayed in the mail or exposed to high temperatures. This may cause a false positive result.

MEDIUM-CHAIN ACYL-COA DEHYDROGENASE (MCAD) DEFICIENCY

Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency is characterized by the inability to produce adequate amounts of an enzyme involved in the metabolism of medium chain fatty acids. Proper production of the MCAD enzyme is critical in the process of providing fuel for the body during extended fasting and times of higher energy demands. If untreated, MCAD deficiency can lead to metabolic failure, seizures, coma and death. Treatment consists of avoidance of fasting by eating frequent meals, reduction of dietary fat, and carnitine supplementation. The *prevalence* of MCAD deficiency in the United States is approximately 1 in 20,000.

Clinical Features

Infants with MCAD deficiency appear normal at birth but develop symptoms between three and 24 months of age in response to either prolonged fasting or common illness. Clinical signs are variable and may be confused with other fatty acid oxidation disorders. Infants may present with hypoglycemia, vomiting, and lethargy, which may progress to seizures, coma, and sudden death. Hepatomegaly and acute liver disease are often present. Approximately 20% of those affected die during the first crisis.

Etiology

MCAD deficiency is caused by a genetic deficiency in the medium-chain acyl-CoA dehydrogenase enzyme, which results in a defect of fatty acid β-oxidation, a major source of energy when the body's hepatic glycogen stores are depleted. MCAD deficiency is inherited in an *autosomal recessive* fashion.

Laboratory Tests

The MCAD deficiency *screening* is done using a technology called tandem mass spectrometry (MS/MS). The levels of octanoyl carnitine (C8) and acyl carnitine (C2) in the blood spot are measured by a tandem mass spectrometer. Infants are considered to have a *presumptive positive* test for MCAD deficiency when they have blood C8 levels of 0.8 μmol/L or more and a C8-to-C2 ratio of 0.02 or greater.

Laboratory Result Classifications and Corresponding Follow-up Actions for MCAD deficiency

Analyte	**Normal Results**	**Borderline Results**	**Presumptive Positive**
Octanoyl carnitine (μmol/L serum)	<0.5	0.5-0.79	≥0.8
	Results are mailed to specimen submitter. No follow-up is required.	If first screen, health care provider is contacted by phone to recommend a repeat newborn screening specimen as soon as possible. If two abnormal screens, diagnostic testing is recommended. Results are also mailed to submitter.	If first screen, health care provider is contacted by phone to recommend immediate second specimen. If two abnormal screens, immediate diagnostic testing is recommended. Results are also mailed to submitter.

Treatment

Treatment for MCAD deficiency is simple and appears to be very effective. Those affected need to avoid fasting by having frequent meals and limit their intake of medium- and long-chain fatty acids. In circumstances where food cannot be tolerated, such as during an illness, intravenous glucose support may be required. Carnitine supplementation is sometimes prescribed to correct for secondary carnitine deficiency and help eliminate toxic metabolites.

False Positive/Negative

Because Washington state recently began screening using tandem mass spectrometry, information about false positive and false negative rates are not available.

HOMOCYSTINURIA

Homocystinuria is characterized by a defect in the metabolism of the amino acid methionine, usually due to a deficiency of the enzyme cystathionine β-synthase. If untreated, approximately 50% of those with homocystinuria die before the age of 25 years, typically from thromboembolic events. Developmental delay, mental retardation, psychiatric disturbances, seizures, displacement of the lens of the eye, nearsightedness, scoliosis and osteoporosis are also commonly present. Initial treatment of homocystinuria consists of providing the baby with a formula that does not contain methionine. A methionine-restricted cysteine-supplemented diet may be required throughout life and administration of vitamin B6 (pyridoxine) is also often prescribed. The *prevalence* homocystinuria in the United States is approximately 1 in 200,000.

Clinical Features

Infants with homocystinuria appear normal at birth and early symptoms of the disorder are indistinct. Delayed development is usually noticed before 3 years of age and nearsightedness is the first sign of lens dislocation. Signs of homocystinuria are similar to that of Marfan syndrome. Besides ocular abnormalities, affected individuals also have tall, thin statures with long limbs, spidery fingers and pectus deformity of the chest. Mental retardation, psychiatric disturbances, and thinning and weakness of the bones are also common. Individuals frequently develop blood clots, which can cause life threatening thromboembolic episodes.

Etiology

Homocystinuria is commonly caused by a genetic deficiency in the enzyme cystathionine β-synthase, which is needed to properly metabolize the amino acid methionine. At least nine genetic defects have been shown to disrupt the major pathway in which methionine is metabolized. Cystathionine β-synthase deficiency is the most common and results in high levels of serum methionine. Homocystinuria is inherited in an *autosomal recessive* fashion.

Laboratory Tests

The homocystinuria deficiency *screening* is done using a technology called tandem mass spectrometry (MS/MS). The level of methionine in the blood spot is measured by a tandem mass spectrometer. Infants are considered to have a *presumptive positive* test for homocystinuria when they have blood methionine levels of 80 μmol/L or more.

Laboratory Result Classifications and Corresponding Follow-up Actions for Homocystinuria

Analyte	Normal Results	Borderline Results	Presumptive Positive
Methionine (μmol/L serum)	< 80	80 – 89	≥ 90
	Results are mailed to specimen submitter. No follow-up is required.	NBS waits for the routine second specimen. If not received within 2 to 4 weeks, health care provider is contacted. If second screen, call health care provider to request a third screen. Results are also mailed to submitter.	If first screen, health care provider is contacted by phone to recommend immediate second specimen. If second screen, immediate diagnostic testing is recommended. Results are also mailed to submitter.

Treatment

Treatment for homocystinuria varies, but usually consists of high doses of vitamin B6, a methionine-restricted, cysteine-supplemented diets, and folic acid supplements. Slightly less than 50% respond to vitamin B6 therapy and those that do, should continue throughout their life. Treatment appears to reduce the risk of thromboembolic episodes, seizures, and mental retardation and delays lens dislocation.

False Positive/Negative

Because Washington state recently began screening using tandem mass spectrometry, information about false positive and false negative rates are not available.

MAPLE SYRUP URINE DISEASE (MSUD)

Maple syrup urine disease (MSUD) is characterized by the inability to metabolize the branched-chain amino acids leucine, isoleucine and valine due to a deficiency of the branched-chain alpha-keto acid dehydrogenase complex. If untreated, the most severe formof MSUD can result in death within the first weeks of life. Less sever forms of MSUD will result in mental retardation and metabolic decompensation during times of stress. Treatment consists of a special diet low in leucine, isoleucine and valine. The *prevalence* MSUD in the United States is approximately 1 in 200,000.

Clinical Features

There are four general classifications used to describe the variants of MSUD: classic, intermediate, intermittent and thiamine-responsive. In the most common type, classic MSUD, infants appear normal at birth but develop symptoms within four to seven days. Symptoms include poor feeding and weight gain, vomiting, lethargy, hypotonia or hypertonia and the characteristic maple syrup smell of their urine. Babies with classic MSUD will die within the first year of life if left untreated.

Etiology

Disorder caused by a genetic deficiency of the branched-chain alpha-keto acid dehydrogenase complex, which is needed to metabolize the essential amino acids leucine, isoleucine and valine. It is inherited in an *autosomal recessive* fashion.

Laboratory Tests

The MSUD deficiency *screening* is done using a technology called tandem mass spectrometry (MS/MS). The levels of leucine, valine and alanine in the blood spot are measured by a tandem mass spectrometer. Infants are considered to have a *presumptive positive* test for MSUD when they have blood leucine levels of 350 μmol/L or more, blood valine levels of 320 μmol/L or more, and a leucine-to-alanine ratio of 1.75 or greater.

Laboratory Result Classifications and Corresponding Follow-up Actions for MSUD

Analyte	Normal Results	Borderline Results	Presumptive Positive
Leucine (μmol/L serum)	< 300	300-349	≥ 350
	Results are mailed to specimen submitter. No follow-up is required.	If first screen, health care provider is contacted by phone to recommend a repeat newborn screening specimen as soon as possible. If two abnormal screens, diagnostic testing is recommended. Results are also mailed to submitter.	Health care provider is called and immediate diagnostic testing is recommended. Results are also mailed to submitter.

Treatment

Treatment of MSUD involves dietary restriction of branched-chain amino acids and requires frequent dietary monitoring that must continue throughout life. Levels of plasma branched-chain amino acids are measured to calculate the appropriate level of dietary restriction required for an individual to avoid symptoms of MSUD without impairing growth and intellectual development. Glucose and insulin infusions are commonly given during episodes of acute metabolic decompensation.

False Positive/Negative

Because Washington state recently began screening using tandem mass spectrometry, information about false positive and false negative rates are not available.

SICKLE CELL DISEASE AND OTHER HEMOGLOBINOPATHIES

Hemoglobinopathies are inherited abnormalities in the structure or amount of hemoglobin. Infants with normal hemoglobin will have a screening result of FA, indicating that both fetal and adult hemoglobin is present. In sickle cell disease the predominant hemoglobin is hemoglobin S (HbS). When oxygenated, HbS functions normally. When under reduced oxygen, it forms crystal-like rods, distorting the red blood cells into a sickle shape. These red blood cells are easily destroyed and tend to stick together, blocking blood vessels. This causes many of the painful symptoms and organ damage associated with sickle cell disease.

The frequency of hemoglobinopathies varies among ethnic groups. Sickle hemoglobin is found most commonly among people with African, Mediterranean, Middle Eastern, and Indian ancestry. In the United States, sickle cell disease is found in virtually all ethnic groups with a *prevalence* of approximately 1 in 10,000 in the general population. However, it is present in approximately 1 in 400 persons of African ancestry. In Washington State, there are, on average, seven infants with sickle cell disease detected each year. In addition, another ten infants are found through newborn hemoglobin *screening* to have other clinically significant hemoglobinopathies such as transfusion dependent thalassemias.

Clinical Features

With the exception of alpha thalassemia major (Fetal Hydrops Syndrome), infants affected with hemoglobinopathies appear normal at birth. With sickle cell disease, anemia develops in the first few months of life as the amount of fetal hemoglobin decreases and HbS increases. Enlargement of the spleen results from the trapping of sickled red blood cells in the spleen. If acute, this can rapidly cause severe anemia and transfusions may be necessary. Splenic sequestration can result in death.

Infants and children with sickle cell disease are particularly susceptible to bacterial infections. This may manifest as pneumonia, meningitis, osteomyelitis, or septicemia. Prompt antibiotic treatment can be lifesaving. Studies have also shown that prophylactic oral penicillin and folic acid started early and maintained through age six, decreases the number of episodes of infections and death.

Health problems due to sickle cell disease are highly variable. Pain is the most common symptom of sickle cell disease. Pain episodes can occur at any time and in any part of the body. However, they occur most often in the arms, legs, chest and abdomen. These episodes vary in frequency, severity, and length. Some individuals rarely have painful episodes; others have them frequently. When they occur, they can last from a few hours to several days and can be severe enough to require hospitalization and the use of very strong pain medication.

Anemia (a low number of red blood cells) is another common medical problem of sickle cell disease. This occurs because sickled red blood cells don’t live as long as normal red

blood cells and a person with sickle cell disease cannot make red blood cells fast enough to keep up with the rapid breakdown.

In the adolescent and adult with sickle cell disease, other complications can occur due to the problems with impaired circulation, the premature breakdown of the red blood cells, and damage to the spleen and other body organs. These include jaundice, slower growth and onset of puberty, fatigue, gallstones, shortness of breath, blood in the urine, and stroke. There is currently no cure for sickle cell disease, but with appropriate medical care and management, the complications of sickle cell disease can be minimized.

The other significant hemoglobinopathies reported by the Newborn Screening Program include hemoglobin C, D, E, and alpha thalassemias which have variable clinical manifestations ranging from mild to severe anemia. All have reproductive implications for families.

Etiology
Normal adult hemoglobin consists of four heme molecules and four globin chains, two alpha and two beta chains. Sickle cell disease is a recessively inherited defect of the beta globin chains. A single replacement of one amino acid in the genetic code of both beta globin chains resulting in two hemoglobin S genes, or hemoglobin S in combination with another abnormal hemoglobin such as C, D or beta thalassemia, causes sickle cell disease.

Other Clinically Significant Hemoglobinopathies
Other clinically significant hemoglobinopathies result when there is an observable change in the alpha or beta globin chain. Thalassemias are caused by decreased synthesis of normal globin chains and therefore decreased production of hemoglobin A.

Carrier Detection (Hemoglobin Traits)
The identification of carriers of hemoglobin traits is a by-product of the *screening* for sickle cell disease and other hemoglobinopathies. The Newborn Screening Program reports all traits detected, including hemoglobin S, C, D, E, Bart's and unidentified variants. Most hemoglobin traits are not associated with clinical symptoms or the need for treatment. However, because they have reproductive implications for the parents and the child, the *health care provider* is notified by mail of trait status and provided with information to share with the family. It is suggested that the parents of a child with a hemoglobin trait should be offered *genetic counseling* and testing to determine if future children are at risk for disease.

Laboratory Tests
Initial hemoglobin *screening* is performed by isoelectric focusing (IEF), in which hemoglobin bands are identified by their migration distance in an electric field. Abnormal findings on IEF are confirmed by High Performance Liquid Chromatography (HPLC). Further analysis by DNA/PCR is available if necessary.

Hemoglobins are by far the most complex of the conditions detected by Newborn Screening. More than a dozen genes are involved in hemoglobin production and nearly 700 abnormalities have been described by researchers and clinicians. Also, a variety of combinations are possible for any individual. Listed in the table below are some of the more commonly seen newborn hemoglobin screening findings:

Laboratory Result Classifications and Corresponding Follow-up Actions

Hemoglobin Result	**Likely Clinical Expression**	**NBS Follow-up Action**
FA	- Normal	None
AF or AA	- Transfusion or Older infant	If transfused, report by letter and recommend rescreening 120 days after last transfusion.
FSS FS- or FSA FSC FSD	- Sickle cell disease - Sickle beta thalassemia - Sickle C disease - Sickle D disease	Contact health care provider (HCP) by phone and recommend immediate referral to a pediatric hematologist.
F only	- Beta thalassemia major	Contact HCP by phone and recommend immediate referral to a pediatric hematologist.
FE- FEE FA + high Bart's FCC FCA	- E-beta thalassemia - Homozygous Hemoglobin E disease - Hemoglobin H disease - Hemoglobin C disease - C-beta thalassemia	Report by letter recommending a diagnostic work-up.
FAS FAE FAC FAD	- Hemoglobin S trait - Hemoglobin E trait - Hemoglobin C trait - Hemoglobin D trait	Report by letter to HCP suggesting family studies and genetic counseling.
FA+Bart's (low or moderate level)	- Alpha thalassemia (silent carrier or trait)	Report by letter to HCP recommending follow-up testing to determine clinical significance for child and reproductive implications for family.
FA + Unidentified Variant Trait	- Benign hemoglobin trait	Report by letter to HCP recommending follow-up only if accompanied by clinical signs or *family history* of hemoglobinopathy.

Treatment
Infants with sickle cell disease should take prophylactic penicillin until the age of six. Parents need education on how to take and respond to a temperature, care for acute illness, and how to assess spleen size. It is also important that affected children receive all recommended vaccinations including the pneumococcal vaccine. Consultation with a pediatric hematologist is strongly advised. In addition, continued family education, support groups, and *genetic counseling* are an important part of treatment for the child and family.

False Positive/Negative
A *false positive* hemoglobin result may occur when beta thalassemia occurs in combination with a structural change in the beta globin chain. For example, a child with hemoglobin S trait may appear to have sickle beta thalassemia due to the biological variation in the switch from fetal to adult hemoglobin. The Newborn Screening Program will provide appropriate recommendations for the follow up of such infants. *False negative* results can result from degradation due to specimen age or unusual storage conditions. Most affected are unstable hemoglobins such as Bart's.

Special Considerations
The newborn screening specimen should be obtained prior to transfusing a newborn. After transfusion the hemoglobin results are masked by the donor's blood and hemoglobin testing is invalid. If the newborn screening specimen is not obtained prior to the transfusion, an additional specimen should be collected 120 days after the last transfusion. However, this should not delay collection of the first and second specimens at the normal recommended times. It is still possible to screen for the other disorders despite the transfusion.

A newborn screening specimen should always be mailed within the 24 hours after it is collected. In addition to possibly unnecessarily delaying diagnosis of one of the disorders screened, a specimen received fourteen days after collection cannot be screened for hemoglobinopathies due to the degradation of the red blood cell. A repeat specimen will be required.

NEWBORN HEARING SCREENING

Hearing loss affects approximately three newborns per one thousand but can often be detected at birth by a simple, inexpensive test performed before hospital discharge. This early detection allows for timely diagnosis and intervention.

Newborn hearing screening is not mandated in Washington State but is currently done in many hospitals for all newborns or those at highest risk for hearing loss. Of 75 birthing hospitals in Washington, 31 had some form of newborn hearing screening in place in 2001. By June 2002, 12 additional hospitals have implemented newborn hearing screening programs. Currently, over 85% of hospital-born infants are screened for hearing loss in Washington.

To increase that number, the *Department of Health* has been funded by grants through the *Centers for Disease Control and Prevention* (CDC) and the *Health Resources and Services Administration* (HRSA) to implement a statewide universal hearing screening program. This program is referred to as Early Hearing Loss, Detection, Diagnosis, and Intervention (EHDDI). As a foundation for EHDDI, the *Department of Health* is developing a surveillance and tracking system to ensure that all infants are screened and, when necessary, continue on for rescreening, diagnosis and intervention. Seven hospitals have been selected to pilot this program in Washington and are helping in the development of a revised Newborn Screening collection card, which will enable documentation of hearing screening results as well. The goal of EHDDI is to screen every infant for hearing loss before hospital discharge or before one month of age.

If you would like information on EHDDI or are interested in establishing a program in your facility, please contact the Washington State Department of Health EHDDI Program, at (253) 395-6729 or ehddi2@doh.wa.gov.

APPENDIX A

UNSUITABLE SPECIMEN CAUSES

The table below lists common causes of unsatisfactory and unsuitable blood specimens received for newborn screening. The reason a specimen is invalid will be noted on the results. An invalid specimen does not complete screening and a repeat specimen should be sent.

INVALID SPECIMEN	POSSIBLE CAUSES
Blood did not completely soak through filter paper	• Making multiple small applications instead of completely filling filter paper circles at once • Blood did not soak through the filter paper to the other side • Using a capillary tube to apply blood
Specimen appears layered, clotted, or supersaturated	• Repeated application of blood to same filter paper circle • Applying blood to both sides of the filter paper • Applying too much blood to the filter paper • Blood clotting in a capillary tube used to apply blood
Specimen surface appears scratched or abraded	• Touching the surface of filter paper while applying blood with a capillary tube
Specimen exhibits serum rings; or appears diluted, discolored or contaminated	• Blood clotted in a capillary tube used to apply blood • Squeezing area surrounding puncture • Improper drying of specimen • Alcohol not completely wiped away or dried before puncturing skin • Specimen exposed to high temperatures • Allowing the filter paper to come into contact with other surfaces or hands
Specimen received in plastic bag	• Specimen received in a sealed plastic bag
Specimen damaged during transport	• Specimen ripped or torn during transport/mailing • Specimen contaminated with water or other liquid during transport/mailing.
No blood	• No blood collected on specimen form • Refusal specimen without a signature obtained
Missing or incomplete name on collection form	• Mother's name not supplied • "Adopted" not written into last name field when child is adopted or in foster care and birth mother's name is not known
Specimen too old for testing	• Specimen was too old for reliable testing (Specimen is too old for hemoglobin screening if received more than 14 days after collection; specimen is too old for all screening if received more than 30 days after collection)
Wet specimen	• Mailing specimen before drying for a minimum of two hours
Specimen submitted on out of date form	• Specimen collected on out of date form (current valid forms are green and purple)

To assist in specimen collection, a colored wall chart similar to the one above is available at no charge ('Simple Spot Check' by Schleicher & Schuell). Please contact the Newborn Screening Program if you are interested.

APPENDIX B

HOW TO CONTACT THE NEWBORN SCREENING PROGRAM

Mailing Address for Correspondence:

Newborn Screening Program
Washington State Department of Health
1610 N.E. 150th Street
Shoreline, WA 98155

Mailing Address for Specimens:

Newborn Screening Laboratory
Washington State Department of Health
PO Box 55729
Shoreline, WA 98155-0729

Phone (206) 361-2902
Fax (206) 361-4996

Washington State Newborn Screening Program Web Site:
http://www.doh.wa.gov/nbs

	Phone	Email Address
Michael Glass, Director	(206) 361-2890	Mike.Glass@doh.wa.gov
Sheila Neier, Follow-up Coordinator	(206) 361-2840	Sheila.Neier@doh.wa.gov
Santosh Shaunak, Laboratory Coordinator	(206) 361-4985	Santosh.Shaunak@doh.wa.gov
Robert Fineman, MD, Medical Consultant		drbob@u.washington.edu

APPENDIX C

DIRECTORY OF AVAILABLE MEDICAL CONSULTANTS AND REFERRALS

Pediatric Endocrinologists for Consultation and Referral for {PRIVATE } Congenital Hypothyroidism (CH) & Congenital Adrenal Hyperplasia (CAH)

WASHINGTON

Meera Ramayya, MD
720 South 320th Street
Federal Way, WA 98003
Phone: (253) 941-9400
Fax: (253) 941-6664

Nikom Wannarachue, MD
721 S. Auburn
Kennewick, WA 99326
Phone: (509) 586-1157
Fax: (509) 582-4189

Diana Tattoni, MD
433 State St.
Kirkland, WA 98033
Phone: (425) 828-3626
Fax: (425) 828-3628

Diana Lindner, MD
(for Group Health patients)
Eastside Primary Care
2701 - 156th Ave. NE
Redmond, WA 98052
Phone: (425) 901-2222
Fax: (425) 556-6024
Endocrine Clinic at Group
Health Central (Seattle):
Phone: (206) 326-3166
Fax: (206) 326-2108

Endocrine Clinic
Children's Hosp. & Medical Center
Gad Kletter, MD - NBS Consultant
Daniel Gunther, MD
Cathy Lum, MD
Catherine Pihoker, MD
Gail Richards, MD
4800 Sand Point Way NE, CH-92
Seattle, WA 98105
Consulting: (206) 987-5037
Appointment: (206) 987-2640
Fax: (206) 987-2720
e-mail: gadi.k@seattlechildrens.org

Jeanne Hassing, MD
Children's Hospital - Spokane
105 W. 8th Ave, Suite 660E
Spokane, WA 99204
Phone: (509) 474-2088

Martin Goldsmith, MD
Pediatrics Northwest
316 South MLK Way, #212
Tacoma, WA 98405
Phone: (253) 383-5777
Fax: (253) 383-5320

Endocrine Clinic
Mary Bridge Children's Hospital
Rogelio Ruvalcaba, MD - Medical Director
311 South L St.
Tacoma, WA 98405
Phone: (253) 552-1415
Fax: (253) 552-4979

Jacqueline Smith, MD
2312 NE 129th Ave., Suite 132
Vancouver, WA 98686
Phone: (360) 576-4309
Fax: (360) 576-4306

Richard Mauseth, MD
1700 - 140th Ave. NE, Suite 102
Woodinville, WA 98072
Phone: (425) 483-5437
Fax: (425) 485-6528

OREGON

Scott Mandel, MD
Kaiser Permanente
4855 Western Ave.
Beaverton, OR 97005
Phone: (503) 350-2442
Fax: (503) 626-4415

Stephen LaFranchi, MD
Department of Pediatrics (CDRCP)
Oregon Health Sciences University
707 SW Gaines Road
Portland, OR 97239
Phone: (503) 494-6430
Fax: (503) 494-4953
Phone: (503) 494-6430
Fax: (503) 494-4953

Physicians With Interest in Hemoglobinopathies and Available for Consultation

Pediatric Hematologists

Michael Bender, MD, PhD
Newborn Screening Program Consultant
Medical Director of Sickle Cell Clinic
Odessa Brown Children's Clinic
2101 East Yesler Way
Seattle, WA 98122
CONSULTING: (206) 667-4125
FAX: (206) 667-4937
APPOINTMENT: (206) 987-7232
E-MAIL: mbender@fhcrc.org

Daniel Niebrugge, M.D.
William Thomas, M.D.
Mary Bridge Children's Hospital
Comprehensive Sickle Cell Clinic
311 South L Street
Tacoma, WA 98405
CONSULTING: (253) 383-5777
FAX: (253) 383-5320
APPOINTMENT: (253) 594-1415

Philip Herzog, M.D.
Ronald R. Louie, M.D.
Group Health Hematology
2700 - 152nd Avenue N.E.
Redmond, WA 98052
PHONE: (425) 883-5564
FAX: (425) 883-5715

Judy Felgenhauer, M.D.
Frank Reynolds, M.D.
Deaconess Medical Center
800 West 5th Avenue
Spokane, WA 99204
PHONE: (509) 458-7230
FAX: (509) 458-7986

Primary Care Physicians

Greg Welsh, M.D.
Madrona Medical Group
3149 Ellis Street, Suite 101
Bellingham, WA 98225
PHONE: (360) 734-4302
FAX: (360) 647-4752

Jane A. Mays, M.D.
Pediatric Associates
1051 NE 7th Avenue
Oak Harbor, WA 98277
PHONE: (360) 679-6166
FAX: (360) 675-0275

Brent Oldham, M.D.
Pacific Medical Clinics
1101 Madison, Suite 301
Seattle, WA 98104
PHONE: (206) 505-1200
FAX: (206) 505-1053

Kenneth Feldman, M.D.
Odessa Brown Children's Clinic
2101 East Yesler Way
Seattle, WA 98122
PHONE: (206) 329-7876
FAX: (206) 329-9764

George Tanbara, M.D.
Pediatrics Northwest
316 South MLK Jr. Way, #212
Tacoma, WA 98405
PHONE: (253) 383-5777
FAX: (253) 383-5320

Genetic Counseling Resources Available for Hemoglobinopathies

Associated with Comprehensive Specialty Hemoglobinopathy Clinic

Roger Fick, MS, CGC
Comprehensive Sickle Cell Program
Mary Bridge Children's Hospital & Health Center
P.O. Box 5299
Tacoma, WA 98405-0987
Phone: (253) 403-3476
Fax: (253) 403-1540

Sheila Neier, MS
Comprehensive Sickle Cell Program
Odessa Brown Children's Clinic
2101 E. Yesler Way
Seattle, WA 98122
Phone: (206) 987-7290
Fax: (206) 329-9764

Melanie Ito, MD, MS, CGC
Columbia Health Center
4400 - 37th South
Seattle, WA 98118
Phone: (206) 296-4650
Fax: (206) 205-6075

General Genetics Clinics

Linda Ramsdell, MS, CGC
Darci Sternan, MS, CGC
Division of Medical Genetics
Children's Hospital & Medical Center
P.O. Box 5371
Seattle, WA 98105-0371
Phone: (206) 526-2056
Fax: (206) 526-2217

Justine Coppinger, MS, CGC
Lael Hinds, MS, CGC
Kathi Marymee, MS, CGC
Inland Northwest Genetics Clinic
2607 Southeast Blvd #A100
Spokane, WA 99223
Phone: (509) 535-2278
Fax: (509) 535-7502

Susie Ball, MS, CGC
Shelly Rudnick, MS, CGC
Central Washington Genetics Program
Yakima Valley Memorial Hospital
2811 Tieton Drive
Yakima, WA 98902
Phone: (509) 575-8160
Fax: (509) 577-5088

Susie Ball, MS, CGC
Genetics Program
Central Washington Hospital
1201 South Miller
Wenatchee, WA 98801
Phone: (509) 667-3350

Pat Cooper, PhD, CGC
Blue Mountain Genetic Counseling
St. Mary Medical Center
P.O. Box 1477
Walla Walla, WA 99362
Phone: (509) 525-1302
Fax: (509) 522-9448

Kathy Leppig, MS, CGC
Lael McAuliffe, MS, CGC
Ute Ochs, MD
Group Health Cooperative
Group Health University Center
4225 Roosevelt Way NE
Seattle, WA 98105
Phone: (206) 634-4036
Services limited to Group Health Members only

Sarah Hall, MS
Madigan Army Medical Center
Developmental Pediatrics
Tacoma, WA 98431-5000
Phone: (253) 968-2310
Fax: (253) 968-0384
Services limited to Armed Services personnel and their dependents only

Robin Bennett, MS, CGC
Whitney Neufeld-Kaiser, MS, CGC
Corinne Smith, MS, CGC
University of Washington Medical Center
Medical Genetics, Box 357720
1959 NE Pacific Street
Seattle, WA 98195-7720
Phone: (206) 616-2135

Prenatal Genetics Clinics

Stefanie Uhrich, MS, CGC
Leslie Carpenter, MS,
Linda Knight, MS
Prenatal Genetics and Fetal Therapy
University of Washington
Box 356159
Seattle, WA 98195
Phone: (206) 598-8130
Fax: (206) 598-2359

Kathleen Hays, MS, CGC
Evergreen Hospital
Maternal-Fetal Medicine
12040 NE 128th Street
Kirkland, WA 98034
Phone: (425) 899-2200
Fax: (425) 889-2210

Gail Hammer, MS
Southwest Washington Perinatal Services
314 Martin Luther King Jr. Way, Suite #402
Tacoma, WA 98405
Phone: (253) 552-1037
Fax: (425) 688-8110

Eastside Maternal-Fetal Medicine Associates
1135 – 116th Ave NE
Overlake Medical Tower
Bellevue, WA 98004
Phone: (425) 688-8111
Fax: (253) 552-1789

Additional Genetic Resources

Washington State Genetic Resource Line: 1-800-562-GENE (4363)
An educational service dedicated to providing health and social service professionals with current information regarding services on human genetics. This service is provided through the Division of Medical Genetics, Department of Medicine, University of Washington.

Cross-Culture Health Care Project
The Cross-Cultural Health Care Project at Pacific Medical Center in Seattle has an extensive library of ethnocultural training and educational resources for medical providers. Staff can be contacted at (206) 326-4161.

Family Planning Toll Free Line: 1-800-770-4334
The toll-free family planning line was created by the Department of Social and Health Services Medical Assistance Administration in conjunction with the Healthy Mothers Healthy Babies Coalition of Washington State and the Department of Health. It was established to implement the 1994 Welfare Reform legislation of increasing awareness, access and availability of family planning services.

Hemoglobinopathy Diagnostic Testing Laboratories

Children's Hospital & Regional Medical Center
4800 Sandpoint Way N.E.
Seattle, WA 98105
(206) 526-2102

Department of Pathology
Providence Seattle Medical Center
500 - 17th Avenue, C34008
Seattle, WA 98124
(206) 320-2649

Hemolysis Laboratory
Department of Laboratory Medicine
University of Washington, Box 357110
Seattle, WA 98195
(206) 548-6230

Laboratory of Pathology of Seattle, Inc.
1229 Madison St., Suite 500
Seattle, WA 98104
(206) 386-3366

Virginia Mason Clinic Lab
1100 - 9th Avenue
Seattle, WA 98101
(206) 223-6899

Quest Diagnostics
18251 Cascade Ave. South
Seattle, WA 98188
(206) 394-1900

Empire Health Laboratories
Deaconess Medical Center
West 800 - 5th Avenue
Spokane, WA 99210-1248
(509) 458-7127

Quest Diagnostics
6600 S.W. Hampton St.
Portland, OR 97223
(503) 306-1000

Sacred Heart Medical Center Lab
101 West 8th, P.O. Box 2555
Spokane, WA 99220
(509) 626-4413

Multicare Medical Center
Tacoma General Hospital Lab
315 South MLK Way
P.O. Box 5299
Tacoma, WA 98405
(253) 552-4848

To be included on this list, a laboratory must hold a current Washington State Laboratory license and successfully participate in a Hemoglobinopathy proficiency testing program such as the College of American Pathologists set HG. No further endorsement is intended or implied. If you have questions, please call Santosh Shaunak, Washington State Newborn Screening laboratory coordinator, at (206) 361-4985.

Follow-up Facilities for Metabolic Disorders

University of Washington PKU Clinic
C. Ronald Scott, M.D. – Clinic Director
Cristine Trahms, MS, RD – Nutrition Consultant
CHDD, Box 357920
University of Washington
Seattle, WA 98195-7920
Program Coordinator – Vicki Frasher
Phone: (206) 685-3015
Fax: (206) 685-1286

Biochemical Genetics Lab
Children's Hospital and Regional Medical Center
Clinical Laboratories
4800 Sand Point Way
Seattle, WA 98105
Phone: (206) 526-2216

APPENDIX D

AVAILABLE PUBLICATIONS AND EDUCATIONAL SERVICES

The following two pages include a list of many of the publications the Newborn Screening Program has available in limited quantities at no charge. The majority of these publications are also available on the Newborn Screening Program web site (www.doh.wa.gov/nbs). In addition, the Newborn Screening Program provides filter paper collection cards, mailing envelopes, and pamphlets free of charge. Please call (206) 361-2902 to order.

The Newborn Screening Program also offers educational in-services to interested institutions. The in-services run approximately 1 to 1 ½ hours and can be tailored to attendees' interests. Topics generally covered include:

- A brief background and history of newborn screening
- The importance of screening
- Information about the disorders screened for in Washington State
- An *NCCLS* video which covers specimen collection and handling
- The role of the hospital in screening

Please contact the Washington State Newborn Screening Program at (206) 361- 2902 if you are interested in this service.

Newborn Screening Publications

Name of Publication	Publication Type	For Parents	For Providers	Language (Other than English)*
Newborn Screening (NBS)				
NBS Blood Specimen Collection and Handling Procedure‡	Poster		✓	1
Simple Spot Check‡	Poster		✓	1
Newborn Screening Tests and Your Baby	Pamphlet	✓		1 - 6
Sickle Cell Disease (SCD)				
Aplastic Crisis	Pamphlet	✓		
Chest Syndrome	Pamphlet	✓		
Comprehensive Sickle Cell Program, Mary Bridge Children's Hospital & Health Center‡	Brochure	✓		
Hemoglobin S	Pamphlet	✓		1
Hemoglobin Sickle C Disease	Pamphlet	✓		
Management and Therapy of Sickle Cell Disease‡	Book		✓	
Pain in the Child with Sickle Cell Disease	Pamphlet	✓		
Parent's Handbook Part 1: Birth to Six Years‡	Book	✓		
Parent's Handbook Part 2: Six to Eighteen Years‡	Book	✓		
Pneumococcal Infection and Penicillin	Pamphlet	✓		
Priapism	Pamphlet	✓		
Sickle Cell Disease in Newborns and Infants: A Guide for Parents‡	Booklet	✓		
Sickle Cell Disease: Birth to Five Years	Wheel	✓		
Sickle Cell Disease: Comprehensive Screening & Management in Newborns and Infants‡	Booklet		✓	
Sickle Cell Disease: Screening, Diagnosis, Management, and Counseling in Newborns and Infants‡	Book		✓	
Sickle Beta Zero Thalassemia	Pamphlet	✓		
Sickle Beta+ Thalassemia	Pamphlet	✓		
Sickle Cell Anemia and Stroke	Pamphlet	✓		
Sickle Cell Anemia: A Parent's Guide for the School Age Child	Pamphlet	✓		
Splenic Sequestration Crisis	Pamphlet	✓		
Thalassemia (Beta)‡	Pamphlet	✓		
Thalassemia Among Asians‡	Pamphlet	✓		2,3,5,6,7
The Sickle Cell Program, Odessa Brown Children's Clinic	Brochure	✓		
The Infant and Young Child with Sickle Cell Anemia	Booklet	✓		1

* 1 = Spanish, 2 = Chinese, 3 = Laotian, 4 = Russian, 5 = Vietnamese, 6 = Cambodian, 7 = Tagalog

‡ Not published by the Washington State Department of Health or affiliated clinical program

Name of Publication	Publication Type	For Parents	For Providers	Language (Other than English)*
Other Hemoglobins				
Alpha Thalassemia	Pamphlet	✓		1,2
Beta Thalassemia	Pamphlet	✓		1,2
Hemoglobin Bart's	Fact Sheet		✓	
Hemoglobin C	Pamphlet	✓		1
Hemoglobin C Disease	Pamphlet	✓		
Hemoglobin C	Fact Sheet		✓	
Hemoglobin D	Pamphlet	✓		
Hemoglobin E	Pamphlet	✓		3,5,6
Hemoglobin E	Fact Sheet		✓	
Phenylketonuria (PKU)				
A Babysitter's Guide to PKU	Booklet	✓		
Chef Lophe's Phe-Nominal Cookbook	Booklet	✓		
Finger Foods Are Fun	Pamphlet	✓		
Games That Teach: Learning by Doing for Preschoolers with PKU	Pamphlet	✓		
New Parents' Guide to PKU	Booklet	✓		
PKU For Children: Learning to Measure	Booklet	✓		
PKU Questions and Answers	Fact Sheet	✓		
What is Phenylketonuria?‡	Pamphlet	✓		1
Why is Mary on a Diet? (Children's Book)	Book	✓		
Information for Adults with PKU:				
Making the Change From High Phe to Low Phe	Booklet	✓		
PKU & Pregnancy: Part 1 General Information‡	Pamphlet	✓		
PKU & Pregnancy: Part 2 Pregnancy Management‡	Pamphlet	✓		
The Essentials of PKU: An Informational Pamphlet for Young Adults with PKU	Booklet	✓		
Congenital Adrenal Hyperplasia (CAH)				
CAH Questions and Answers	Fact Sheet	✓		
CAH Answers‡	Pamphlet	✓		
CAH – Information for Parents‡	Booklet	✓		1
Congenital Hypothyroidism (CH)				
CH Questions and Answers	Fact Sheet	✓		
CH Developmental Evaluation Clinic	Fact Sheet	✓		1
Hypothyroidism and Your Infant‡	Booklet	✓		1

* 1 = Spanish, 2 = Chinese, 3 = Laotian, 4 = Russian, 5 = Vietnamese, 6 = Cambodian, 7 = Tagalog

‡ Not published by the Washington State Department of Health or affiliated clinical program

APPENDIX E

WASHINGTON STATE NEWBORN SCREENING STATUTE AND REGULATIONS

Chapter 70.83 RCW
PHENYLKETONURIA AND OTHER PREVENTABLE HERITABLE DISORDERS

SECTIONS

NOTES:

Reviser's note: Powers and duties of the department of social and health services and the secretary of social and health services transferred to the department of health and the secretary of health. See RCW 43.70.060.

RCW 70.83.010
Declaration of policy and purpose.

It is hereby declared to be the policy of the state of Washington to make every effort to detect as early as feasible and to prevent where possible phenylketonuria and other preventable heritable disorders leading to developmental disabilities or physical defects.

[1977 ex.s. c 80 § 40; 1967 c 82 § 1.]

NOTES:

Purpose -- Intent -- Severability -- 1977 ex.s. c 80: See notes following RCW 4.16.190.

RCW 70.83.020
Screening tests of newborn infants.

It shall be the duty of the department of health to require screening tests of all newborn infants before they are discharged from the hospital for the detection of phenylketonuria and other heritable or metabolic disorders leading to mental retardation or physical defects as defined by the state board of health: PROVIDED, That no such tests shall be given to any newborn infant whose parents or guardian object thereto on the grounds that such tests conflict with their religious tenets and practices.

[1991 c 3 § 348; 1975-'76 2nd ex.s. c 27 § 1; 1967 c 82 § 2.]

RCW 70.83.030
Report of positive test to department of health.

Laboratories, attending physicians, hospital administrators, or other persons performing or requesting the performance of tests for phenylketonuria shall report to the department of health all positive tests. The state board of health by rule shall, when it deems appropriate, require that positive tests for other heritable and metabolic disorders covered by this chapter be reported to the state department of health by such persons or agencies requesting or performing such tests.

[1991 c 3 § 349; 1979 c 141 § 113; 1967 c 82 § 3.]

RCW 70.83.040
Services and facilities of state agencies made available to families and physicians -- Fees.

When notified of positive screening tests, the state department of health shall offer the use of its services and facilities, designed to prevent mental retardation or physical defects in such children, to the attending physician, or the parents of the newborn child if no attending physician can be identified.

The services and facilities of the department, and other state and local agencies cooperating with the department in carrying out programs of detection and prevention of mental retardation and physical defects shall be made available to the family and physician to the extent required in order to carry out the intent of this chapter and within the availability of funds. The department has the authority to collect a reasonable fee, from the parents or other responsible party of each infant screened to fund specialty clinics that provide treatment services for hemoglobin diseases, phenylketonuria, congenital adrenal hyperplasia, and congenital hypothyroidism. The fee may be collected through the facility where the screening specimen is obtained.

[1999 c 76 § 1; 1991 c 3 § 350; 1979 c 141 § 114; 1967 c 82 § 4.]

RCW 70.83.050
Rules and regulations to be adopted by state board of health.

The state board of health shall adopt rules and regulations necessary to carry out the intent of this chapter.

[1967 c 82 § 5.]

Chapter 246-650 WAC
NEWBORN SCREENING

Last Update: 11/24/03

WAC SECTIONS

WAC 246-650-001 Purpose. The purpose of this chapter is to establish board rules to detect, in newborns, congenital disorders leading to developmental impairment or physical disabilities as required by RCW 70.83.050 and to provide protections for the confidentiality of information and human biological specimens submitted pursuant to these requirements.

[Statutory Authority: Chapters 70.83, 43.20 RCW. 03-24-026, § 246-650-001, filed 11/24/03, effective 12/25/03. Statutory Authority: RCW 43.20.050. 91-02-051 (Order 124B), recodified as § 246-650-001, filed 12/27/90, effective 1/31/91. Statutory Authority: RCW 43.20.050 and 70.83.050. 87-11-040 (Order 303), § 248-103-001, filed 5/18/87.]

WAC 246-650-010 Definitions. For the purposes of this chapter:

(1) "Board" means the Washington state board of health.

(2) "Biotinidase deficiency" means a deficiency of an enzyme (biotinidase) that facilitates the body's recycling of biotin. The result is biotin deficiency, which if undetected and untreated, may result in severe neurological damage or death.

(3) "Congenital adrenal hyperplasia" means a severe disorder of adrenal steroid metabolism which may result in death of an infant during the neonatal period if undetected and untreated.

(4) "Congenital hypothyroidism" means a disorder of thyroid function during the

neonatal period causing impaired mental functioning if undetected and untreated.

(5) "Department" means the Washington state department of health.

(6) "Galactosemia" means a deficiency of enzymes that help the body convert the simple sugar galactose into glucose resulting in a buildup of galactose and galactose-1-PO_4 in the blood. If undetected and untreated, accumulated galactose-1-PO_4 may cause significant tissue and organ damage often leading to sepsis and death.

(7) "Homocystinuria" means deficiency of enzymes necessary to break down or recycle the amino acid homocysteine resulting in a buildup of methionine and homocysteine. If undetected and untreated may cause thromboembolism, mental and physical disabilities.

(8) "Maple syrup urine disease" (MSUD) means deficiency of enzymes necessary to breakdown the branch chained amino acids leucine, isoleucine, and valine resulting in a buildup of these and metabolic intermediates in the blood. If undetected and untreated may result in mental and physical retardation or death.

(9) "Medium chain acyl-coA dehydrogenase deficiency" (MCADD) means deficiency of an enzyme (medium chain acyl-coA dehydrogenase) necessary to breakdown medium chain length fatty acids. If undetected and untreated, fasting, infection or stress may trigger acute hypoglycemia leading to physical and neurological damage or death.

(10) "Newborn" means an infant born in a hospital in the state of Washington prior to discharge from the hospital of birth or transfer.

(11) "Newborn screening specimen/information form" means the information form provided by the department including the filter paper portion and associated dried blood spots. A specimen/information form containing patient information is "Health care information" as defined by the Uniform Healthcare Information Act, RCW 70.02.010(6).

(12) "Phenylketonuria" (PKU) means a deficiency of an enzyme necessary to convert the amino acid phenylalanine into tyrosine resulting in a buildup of phenylalanine in the blood. If undetected and untreated may cause severely impaired mental functioning.

(13) "Hemoglobinopathy" means a hereditary blood disorder caused by genetic alteration of hemoglobin which results in characteristic clinical and laboratory abnormalities and which leads to developmental impairment or physical disabilities.

(14) "Significant screening test result" means a laboratory test result indicating a suspicion of abnormality and requiring further diagnostic evaluation of the involved infant for the specific disorder.

[Statutory Authority: Chapters 70.83, 43.20 RCW. 03-24-026, § 246-650-010, filed 11/24/03, effective 12/25/03. Statutory Authority: RCW 43.20.050. 91-02-051 (Order 124B), recodified as § 246-650-010, filed 12/27/90, effective 1/31/91. Statutory Authority: Chapters 43.20 and 70.83 RCW. 91-01-032 (Order 114B), § 248-103-010, filed 12/11/90, effective 1/11/91. Statutory Authority: RCW 43.20.050 and 70.83.050. 87-11-040 (Order 303), § 248-103-010, filed 5/18/87.]

WAC 246-650-020 Performance of screening tests. (1) Hospitals providing birth and delivery services or neonatal care to infants shall:

(a) Inform parents or responsible parties, by providing a departmental information pamphlet or by other means, of:

(i) The purpose of screening newborns for congenital disorders,

(ii) Disorders of concern as listed in WAC 246-650-020(2),

(iii) The requirement for newborn screening, and

(iv) The legal right of parents or responsible parties to refuse testing because of religious tenets or practices as specified in RCW 70.83.020, and

(v) The specimen storage, retention and access requirements specified in WAC 246-650-050.

(b) Obtain a blood specimen for laboratory testing as specified by the department from each newborn prior to discharge from the hospital or, if not yet discharged, no later than five days of age.

(c) Use department-approved newborn screening specimen/information forms and directions for obtaining specimens.

(d) Enter all identifying and related information required on the specimen/information form following directions of the department.

(e) In the event a parent or responsible party refuses to allow newborn screening, obtain signatures from parents or responsible parties on the department specimen/information form.

(f) Forward the specimen/information form with dried blood spots or signed refusal to the Washington state public health laboratory no later than the day after collection or refusal signature.

(2) Upon receipt of specimens, the department shall:

(a) Perform appropriate screening tests for:

(i) Phenylketonuria, congenital hypothyroidism, congenital adrenal hyperplasia, and hemoglobinopathies,

(ii) Biotinidase deficiency, galactosemia, homocystinuria, maple syrup urine disease and medium chain acyl-coA dehydrogenase deficiency according to the schedule in WAC 246-650-030;

(b) Report significant screening test results to the infant's attending physician or family if an attending physician cannot be identified; and

(c) Offer diagnostic and treatment resources of the department to physicians attending infants with presumptive positive screening tests within limits determined by the department.

[Statutory Authority: Chapters 70.83, 43.20 RCW. 03-24-026, § 246-650-020, filed 11/24/03, effective 12/25/03. Statutory Authority: RCW 43.20.050 and 70.83.050. 92-02-019 (Order 225B), § 246-650-020, filed 12/23/91, effective 1/23/92. Statutory Authority: RCW 43.20.050. 91-02-051 (Order 124B), recodified as § 246-650-020, filed 12/27/90, effective 1/31/91. Statutory Authority: Chapters 43.20 and 70.83 RCW. 91-01-032 (Order 114B), § 248-103-020, filed 12/11/90, effective 1/11/91. Statutory Authority: RCW 43.20.050 and 70.83.050. 87-11-040 (Order 303), § 248-103-020, filed 5/18/87.]

WAC 246-650-030 Implementation of screening to detect biotinidase deficiency, galactosemia, homocystinuria, maple syrup urine disease and medium chain acyl-coA dehydrogenase deficiency. The department shall implement screening tests for biotinidase deficiency, galactosemia, homocystinuria, maple syrup urine disease and medium chain acyl-coA dehydrogenase deficiency beginning in January 2004. Screening for these disorders shall be fully implemented as quickly as feasible and not later than

June 2004.

[Statutory Authority: Chapters 70.83, 43.20 RCW. 03-24-026, § 246-650-030, filed 11/24/03, effective 12/25/03. Statutory Authority: RCW 43.20.050. 91-02-051 (Order 124B), recodified as § 246-650-030, filed 12/27/90, effective 1/31/91. Statutory Authority: Chapters 43.20 and 70.83 RCW. 91-01-032 (Order 114B), § 248-103-040, filed 12/11/90, effective 1/11/91.]

WAC 246-650-040 Report to the board. The department shall report to the board annually the following information concerning tests conducted pursuant to this section:

(1) The costs of tests as charged by the department;

(2) The results of each category of tests, by county of birth and ethnic group, as reported on the newborn screening form and, if available, birth certificates; and

(3) Follow-up procedures and the results of such follow-up procedures.

[Statutory Authority: Chapters 70.83, 43.20 RCW. 03-24-026, § 246-650-040, filed 11/24/03, effective 12/25/03.]

WAC 246-650-050 Privacy and security of screening specimen/information forms. The specimen/information form submitted to the department pursuant to WAC 246-650-020 becomes the property of the state of Washington upon receipt by the Washington state public health laboratory. The department shall protect the privacy of newborns and their families and assure that all specimen/information forms submitted for screening are protected from inappropriate use or access.

(1) Storage: The specimen/information forms shall be kept at ambient temperature in secured storage to preserve their confidentiality and prevent access by unauthorized persons.

(2) Retention/destruction: The specimen/information form shall be retained until the child is twenty-one years old in accordance with the requirements for hospitals specified in RCW 70.41.190. After this time the form will be destroyed.

EXCEPTION FOR PARENTAL REQUEST: Upon request of a parent or guardian (or a patient who is over the age of eighteen years), the department will destroy the specimen/information form only after all required screening tests have been performed and if the patient's screening/clinical status related to these tests is not in question.

(3) Access: Access to stored specimen/information forms shall be restricted to department employees and those contractors or others approved by the department as necessary to meet specific program needs. Access is contingent upon compliance with all applicable federal and state laws, regulations, and policies safeguarding the privacy and confidentiality of medical information. The department shall assure that those granted access understand the confidentiality requirements and have a signed confidentiality agreement on file.

(4) Release: Dried blood spot samples and specimen information may only be released when required by state or federal law or under the following conditions:

(a) A sample from a specimen and copies of associated information (patient information and testing results, if requested) may be released to:

(i) A health care provider at the request of the patient or their legal representative after completing and signing a written request form approved by the department. The release

form must be provided to the director of newborn screening before the request will be fulfilled.

(ii) A researcher with the written, informed consent of the patient or their patient's legal representative as part of a research project that has been reviewed and approved by the DOH/DSHS human subjects research review board and the secretary or designee of the department of health.

(iii) A named person in a legally executed subpoena following review and approval of the state attorney general.

(iv) A person to whom release is mandated by order of a court of competent jurisdiction.

(b) Anonymous samples may be released if the department determines that the intended use has significant potential health benefit and that each of the following criteria have been met:

(i) The investigation design is adequate to assure anonymity will be preserved.

(ii) All newborn screening tests have been completed and the status of the infant is resolved.

(iii) At least one fully adequate spot will remain after the anonymous sample has been taken.

(iv) Sufficient resources (personnel) are available for extracting the samples.

(v) The DOH/DSHS human subjects research review board has reviewed and approved the investigation. This requirement may be waived by the department for a very small (i.e., less than 100 sample) pilot study where the intent is to evaluate a testing tool, as opposed to an evaluation where the intent is to measure some characteristic of a population.

(5) Notification: The department shall notify parents of the specimen storage, retention/destruction and access requirements through the department's newborn screening informational pamphlet.

[Statutory Authority: Chapters 70.83, 43.20 RCW. 03-24-026, § 246-650-050, filed 11/24/03, effective 12/25/03.]

WAC 246-650-990 Screening charge. The department has authority under RCW 43.20B.020 to require a reasonable charge from parents or responsible parties for the costs of newborn screening. The charge is to be collected through the facility where the specimen was obtained.

[Statutory Authority: RCW 70.83.040. 99-20-036, § 246-650-990, filed 9/29/99, effective 10/30/99. Statutory Authority: RCW 43.20B.020. 92-02-018 (Order 224), § 246-650-990, filed 12/23/91, effective 1/23/92. Statutory Authority: RCW 43.20.050. 91-02-051 (Order 124B), recodified as § 246-650-990, filed 12/27/90, effective 1/31/91. Statutory Authority: RCW 43.20.050 and 70.83.050. 87-11-040 (Order 303), § 248-103-030, filed 5/18/87.]

WAC 246-650-991 Specialty clinic support fee. The department has the authority under RCW 70.83.040 to collect a fee for each infant screened to fund specialty clinics that provide treatment services for hemoglobin diseases, phenylketonuria, congenital adrenal hyperplasia and congenital hypothyroidism. The specialty clinic support fee is

$3.50. It is to be collected in conjunction with the screening charge from the parents or other responsible party through the facility where the screening specimen is obtained.

[Statutory Authority: RCW 70.83.040. 99-20-036, § 246-650-991, filed 9/29/99, effective 10/30/99.]

APPENDIX F

GLOSSARY OF *ITALICIZED* TERMS

abnormal screening test	any result that is not normal; includes hemoglobin traits and disease, borderline levels, presumptive positive levels, and unsuitable specimens
analyte	a chemical component of the blood (or other body fluid) that is being analyzed
autosomal recessive	the affected individual has a "double dose" of the abnormal gene (on one of the 22 pairs of non-sex chromosomes); the parents are each carriers and show no evidence of the disorder
batching	holding on to NBS specimens for several days to mail to the State Lab at once, rather than mailing the specimen within 24 hours of collection as mandated
borderline	a level that is above the normal analyte range but is not elevated to the level that requires immediate diagnostic testing; in general a second NBS specimen is all that is required to resolve a borderline level; these are evaluated within the Newborn Screening Program and established through experience
Centers for Disease Control and Prevention (CDC)	the federal agency whose goal is to protect the nation's public health by providing guidance in the prevention and control of communicable and other diseases and responding to national public health emergencies; based in Atlanta, Georgia (www.cdc.gov)
cost-benefit	determined by economic analysis, the monetary value of all cost and benefits expressed as dollars of benefit per dollars expended
cost-effectiveness	determined by economic analysis, a health outcome per cost expended
demographic information	data that is provided on the newborn screening filter paper card that identifies the specimen, such as mother's name, baby's birth date, and baby's name
diagnostic testing	further testing that is required after a positive screening test result to confirm or rule out a disorder; this testing is not covered by the newborn screening fee
expanded screening	newborn screening that may detect other disorders not covered by the state screening program
false negative	a screening result that indicated the person is not affected with a disorder which is later shown to be incorrect
false positive	a screening result that indicated the person is affected with a disorder which is later shown to be incorrect

	which is later shown to be incorrect
family history	the known presence of a disorder in one or more blood relatives, which may put one at higher risk for developing that disorder
follow-up	follow-up is an important part of newborn screening; follow-up staff work to verify complete testing of all babies born in Washington, report abnormal results to health care providers, make referrals for diagnostic testing, and educate and support health care providers and families
genetic counseling	meeting with someone knowledgeable in genetics to discuss information and risks about an inherited condition
genotype	the genetic makeup of an individual
health care provider	the individual who provides medical care to a patient, which can include physicians, nurses, and midwives; the primary provider is often determined by one's insurance
Health Resources and Services Administration (HRSA)	a federal agency within the U.S. Department of Health and Human Services whose goal is to "improve and expand access to quality health care for all" (www.hrsa.gov)
Hispanic ethnicity	a person of Mexican, Puerto Rican, Cuban, Central or South American or other Spanish Culture or origin, regardless of race, as defined by the Race and Ethnic Standards for Federal Statistics and Administrative Reporting, adopted on May 12, 1977
incidence	a measure of disease in the population, generally the number of new cases detected over a specified period of time
March of Dimes	a non-profit nationwide agency whose mission is to improve the health of babies by preventing birth defects and infant mortality through four goals: reduce birth defects by ten percent; reduce infant mortality to 7 per 1,000 live births; reduce low birth weight to no more than five percent of all live births; and increase the number of women who get prenatal care in the first trimester to 90 percent (www.modimes.org)
National Committee for Clinical Laboratory Standards (NCCLS)	a globally recognized, voluntary consensus standards-developing organization that works to enhance the value of medical testing within the healthcare community through the development and dissemination of standards, guidelines, and best practices (www.nccls.org)

newborn screening cards	specially designed filter paper cards used for collecting heel stick blood specimens; contains data fields about the mother, baby, and submitter and/or health care provider; the cards are available at no charge through the Newborn Screening Program and should only be used to submit newborn screening specimens to the State Lab
normal ranges	analyte levels that indicate the lack of disease; these are evaluated within the Newborn Screening Program and established through experience
phenotype	the manifestation of an individual's genotype(s)
population-based screening	screening the general population for a disorder rather than only those considered at highest risk; newborn screening is population-based
presumptive positive	analyte levels that indicate the high likelihood of disease which is followed by diagnostic testing; these are evaluated within the Newborn Screening Program and established through experience
prevalence	a measure of the burden of disease in a population; generally the number of cases at a specified point in time or period of time
public health	efforts undertaken by society to protect the health of the general public by assuring conditions in which people can be healthy; examples of public health activities are water quality monitoring, bioterrorism preparation and response, and newborn screening
risk-based screening	screening only those who have been shown to have the highest likelihood of developing a particular disorder, rather than screening the general population
screening	a screening test finds those at risk for a disorder; further diagnostic testing is needed for confirmation
sensitivity	the proportion of individuals with positive screening results among those that are true positives
serum rings	occur when blood collected by a capillary tube clots within the tube prior to application or by excessive milking of the foot during sample application
specificity	the proportion of individuals with negative screening results among those that are true negatives
state lab number	an accession number that is assigned by the State Lab when a specimen is received and is used for tracking purposes; it is composed of the four digit year it was received, the three digit Julian date it was received, and a four digit sequential number

unsuitable	the classification of specimens of unsatisfactory quality or quantity that the Newborn Screening Program receives; these specimens are tested for extreme analyte values but results are not released due to unreliability
Washington State Department of Health	the state agency whose goal is "to protect and improve the health of people in Washington State"; the Newborn Screening Program is within the Epidemiology, Health Statistics, and Public Health Laboratories division of the agency (www.doh.wa.gov)
Washington State Newborn Screening Program	a program within the Department of Health and the Epidemiology, Health Statistics, and Public Health Laboratories division that screens infants born in Washington State for congenital disorders; the detection of these disorders will allow treatment to prevent the morbidity and mortality associated with them (www.doh.wa.gov/nbs)